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STUDIES OF PERIPHERAL VASCULAR RESISTANCE ASSOCIATED WITH TOTAL CARDIOPULMONARY BYPASS

I. Peripheral Resistance Under Condition of Normothermia and Normotension

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THE AVAILABILITY of a satisfactory apparatus for conducting whole body perfusion has stimulated the development of a variety of techniques by different laboratories. Perfusion has been governed by attempting to control one or more physiologic modalities, including arterial flow rate, arterial blood pressure, venous oxygen tension, etc. However, it has been the common experience of numerous investigators that linear relationships between the modalities do not always occur. The failure of some of these linear relationships to remain parallel throughout total body perfusion has been credited in the past to changes in vasomotor tone. Alteration in vasomotor tone produces changes in total peripheral resistance which have been studied by several investigators.[1-5] Read and associates[5] studied the effects of alterations in vasomotor tone in both total peripheral resistance and pressure flow relationships in dogs undergoing total body perfusion by surgical ablation of the central nervous system or administration of vaso-active drugs. It was their opinion that total peripheral resistance in the intact state is made up of several components of

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approximately equal magnitude, namely, nervous influences, inherent myogenic vascular tone, viscous properties of blood, and dimensional considerations in the completely relaxed vessels. McGoon and associates[3] studied 3 patients undergoing total body perfusion and found that mean arterial blood pressure became subnormal at the start of perfusion but returned progressively toward normal as the result of an increasing peripheral vascular resistance. These patients were perfused at normothermia utilizing a blood flow rate of approximately 2.3 L. per square meter of body surface per minute.

The purpose of the present study was to ascertain the change in peripheral vascular resistance associated with total body perfusion carried out under normothermic conditions and with the arterial flow rate adjusted to maintain a relatively normal arterial blood pressure.

METHODS

Eighteen dogs whose weights ranged from 11.0 to 16.5 kilograms (average 13.0 Kg.) were lightly anesthetized with thiopental sodium. Polyethylene cannulas were then inserted into the left femoral artery and vein. These cannulas were connected to Statham strain gauges for pressure recordings. The carotid artery was isolated in the neck for eventual insertion of the inflow cannula. A right thoracotomy through the fifth intercostal space was performed, after which the pulmonary artery was dissected from the aorta and the cardiac output measured. This measurement, using the Bowman Gray square wave electromagnetic flowmeter, has been previously described[6] and consists of the placement of a noncannulating flow probe around the ascending aorta to allow the measurement of ascending aortic flow. Studies were then begun by recording cardiac output (with the exception of coronary flow), arterial pressure, venous pressure, electroencephalogram, and electrocardiogram on a multichannel recorder.

The arterial inflow line from the rotating disc oxygenator was inserted into the carotid artery, after which a single 5/8 inch outflow cannula was placed through the right atrial wall extending into the right ventricular cavity. Total cardiopulmonary bypass was begun with the pulmonary artery completely occluded either by tape or clamp. Similar monitoring of the above-mentioned modalities was carried out during the entire period of bypass with the exception that, during bypass, flow was measured on the arterial line of the bypass unit using the same electromagnetic flowmeter.[7, 8] During perfusion arterial pressure was maintained within 20 mm. of values before bypass by adjusting pump speed. Temperature was controlled within 2.5° C. by means of the Brown-Emmons heat exchanger inserted in the arterial line. Following a 30-minute perfusion, attempts were made to equilibrate pre-prefusion blood volume in the animal with blood from the oxygenator. Monitoring was continued and repeat aortic flows were measured in the ascending aorta for periods of 30 minutes to 1 hour after bypass. At intervals throughout the procedure, blood samples were drawn for oxygen content, pH, and hematocrit. All animals were sacrificed following the completion of the experiments.

Approximately 50 points were selected at appropriate intervals on the monitor record, pressures and flows were calculated, and total peripheral resistance calculated from the formula:

$$\frac{\text{Mean arterial pressure (mm. Hg)} - \text{Mean venous pressure (mm. Hg)}}{\text{Blood flow (ml./min.)}}.$$

The results of these studies have been plotted in graph form to depict changes which occurred.

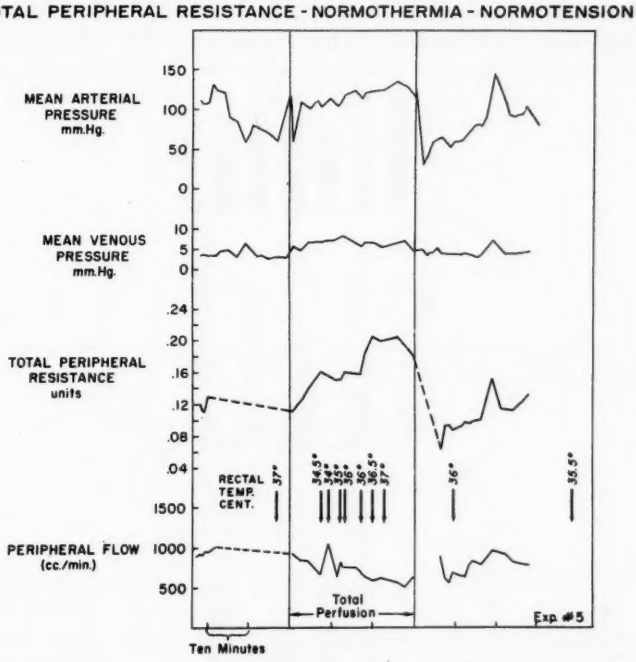

Fig. 1.—This graph was formed from points selected at regular intervals from the monitor record. Note the rise in resistance during bypass and immediate fall afterward.

RESULTS

Eight studies were discarded because of technical reasons which made the experiment inadequate. The reasons usually centered around sequestration of blood in the portal vascular bed and/or abnormally high rises in venous pressure. Fig. 1 depicts a typical experimental record showing arterial and venous pressures, flow rates before, during, and after bypass, and calculated vascular peripheral resistances. Of note in this record, as well as in others, is the drop in arterial blood pressure just prior to institution of total bypass due to interference with venous return at the insertion of venous catheters.

It can be seen that the average cardiac output in these animals falls somewhat below established norms as measured in our laboratory as well as by others. A comparison of the average cardiac output, as measured by the

flowmeter with the output of the pump during bypass, can be seen in Fig. 2 which demonstrates in general the diminution in flow as governed by the conditions of these experiments.

Average peripheral vascular resistance units have been calculated for the period prior to bypass, the first 15 minutes of bypass, and the second 15

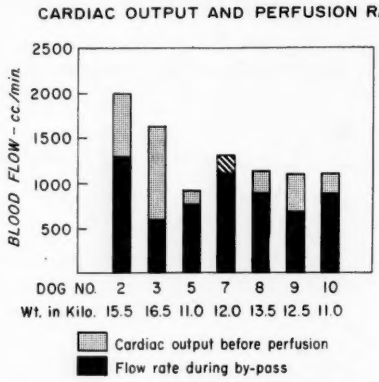

Fig. 2.—These experiments demonstrate the decrease in flow rate during perfusion as compared with cardiac output before bypass. Dog 7 is the lone exception where perfusion rate actually exceeded cardiac output slightly.

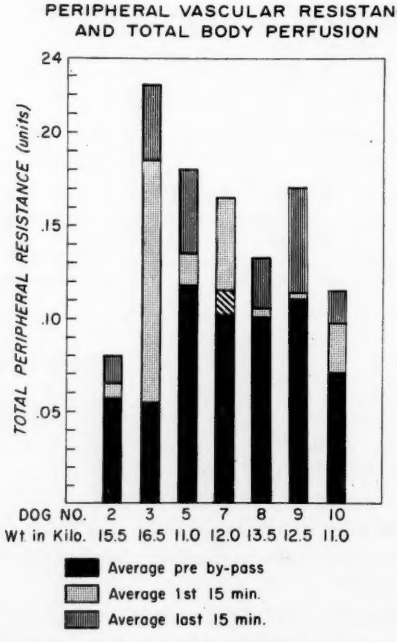

Fig. 3.—These experiments show the characteristic increase in resistance during the period of bypass. Dog 7 developed increased resistance initially but showed a fall below pre-bypass levels toward the end of perfusion.

minutes of bypass, and are shown on Fig. 3. These typical experiments show a uniform increase in peripheral vascular resistance which becomes more marked toward the latter period of the bypass, except for experiment 7 which showed a slight fall in peripheral resistance after an initial rise. The reason for this finding has not been explained on the basis of conditions of the experiment in that this animal was subjected to the same standard conditions as all others.

Total oxygen consumption has been averaged from the determinations made both before and during bypass to allow a comparison of these figures as shown in Fig. 4. Under the conditions of these experiments it can be seen that there was a significant decrease in oxygen utilization during bypass as compared with the period before bypass.

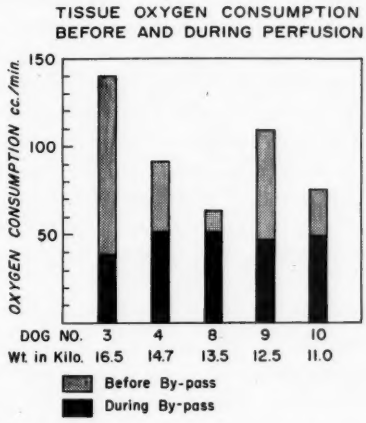

Fig. 4.—Oxygen consumption (calculated from arteriovenous difference and flow rate) consistently fell in all experiments during perfusion as shown in this graph. In some instances (Nos. 3 and 9), this reduction amounted to more than 50 per cent.

pH values were consistently in the alkalotic range before bypass and, in general, came back toward normal levels during the bypass. The lowest pH recorded during bypass in any of these experiments was 7.32 and this level was maintained for only 5 minutes prior to a rise toward normal levels. pH values generally dropped toward the acidotic range in the period immediately after bypass and in a few experiments were in the range of 7.29 within 30 minutes after bypass. Carbon dioxide content was not measured frequently enough to allow adequate study of buffer base values.

COMMENTS

It is of interest that the average cardiac output from these animals as measured before bypass is below levels considered to be normal as measured by the Fick principle and by inlying flowmeter probes in awake animals. Presumably, diminution in cardiac output is produced to some extent by anesthesia and, in part, by thoracotomy and dissection around the great vessels. It was considered in these experiments that blood loss per se was

not a major factor, in view of the fact that great care was taken to assure adequate hemostasis with minimal blood loss during the procedure. On the other hand, flow required to maintain normotension within the given limits during bypass generally fell far below the cardiac output before bypass. According to our current concepts of bypass management, these animals certainly underwent low flows during these experiments. Further evidence of low flow is mirrored by the diminution of oxygen consumption, as well as a tendency toward increasing A-V difference during the bypass.

Elevated pH figures before bypass were almost certainly due to hyperventilation with removal of carbon dioxide and development of a respiratory alkalosis. Since 100 per cent oxygen was used in the oxygenator, we can assume that the maintenance of normal pH during the period of bypass was in a large part due to hypocapnea. This "false" pH maintenance and its ability to mask a progressive metabolic acidosis has been emphasized by Moore.[9]

The rise in peripheral vascular resistance in this study is possibly related to the above-mentioned low flows with attendant development of oxygen debt during perfusion. It is well known that prolonged hypoxia eventually leads to vasodilatation with a pronounced drop in peripheral resistance as seen in severe hemorrhagic and/or traumatic shock. However, in view of the fact that these perfusions were of relatively short duration, it might be that the initial change is one of an increase in peripheral resistance which could be seen to fall if conditions of perfusion were allowed to prevail for a longer period.

It is of interest that this elevated total resistance dropped promptly upon returning the circulation to the animal's heart and lungs. Ankeney[1] has found this same phenomenon in dogs when they were perfused with low flow rates (50 c.c./Kg./min.). He believes that it reflects pooling in inaccessible vascular beds.

Another possible explanation for the increasing peripheral vascular resistance during total body perfusion is that afferent vagal endings situated in the right atrium cause a generalized vagal type constriction as a result of the fall in venous pressure in the atrium brought by the nature of venous cannulation itself. This reflex is thought to be responsible in part for the vasoconstriction which occurs as the usual response to hemorrhage and surgical shock.[10] Both of these conditions are associated with fall in venous pressure.

The well-known tendency of the dog to sequestrate blood in the portal system was seen in some of these experiments. All studies were discarded when significant blood loss from the oxygenator, or hepatic engorgement, or abnormal rise in inferior vena caval pressure was demonstrated. Nevertheless, minor degrees of sequestration could occur and conceivably could contribute to changes in peripheral resistance as seen here.

CONCLUSIONS

1. The governing of total cardiopulmonary bypass solely by maintenance of pre-bypass arterial pressure is by no means a safe criterion of adequate total body perfusion.

2. Under conditions of normothermia and normotension during total cardiopulmonary bypass in the dog, total peripheral vascular resistance tends to increase during a 30-minute bypass period and to drop sharply immediately upon returning circulation to normal.

3. Under these conditions arterial blood flow corresponding to cardiac output is materially reduced over basal cardiac output before bypass.

4. A marked decrease in oxygen uptake by the tissues during the bypass reflects this diminution in arterial flow.

5. Apparently adequate pH range can be maintained under the conditions of these experiments for periods of 30 minutes, but this pH range might well be maintained "falsely" by diminution in carbon dioxide partial pressure.

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DISCUSSION

DR. C. FREDERICK KITTLE, Kansas City, Kans.—Dr. Adams, the previous paper and the discussers have placed particular stress on the arterial side of the vascular unit that is being perfused. I should like to call attention to the fact that this is not a singular vascular unit, but is, actually, a series of units, each with various factors controlling not only the arterioles but also the capillaries and veins.

We have approached the problem of attempting to segregate these by delineating the factors responsible for the return of blood from the inferior and the superior venae cavae.

One can determine the relative per cent of venous return through these two main parts of the body. Then by altering the flow rate of the pump, by the administration of

drugs, by lowering the body temperature, or by producing hypoxia, one can determine various regional factors controlling resistance.

Very briefly, we have found that, although the perfusion rate remains constant, so that the total venous return is constant, the administration of neosynephrine, for instance, results in a relative and absolute increase of flow through the superior vena cava. Arfonad and hypoxia have a similar action.

I am calling attention to this because various regional manifestations may be important with long-term perfusion, or with perfusion at lower temperatures, more so than is presently recognized.

DR. DWIGHT C. MC GOON, Rochester, Minn.—This excellent paper by Dr. Cordell, as well as the final paper by Dr. Sanger, in addition to the many remarks of the various discussers of these papers have indicated that the perfused body is subject to variations in vasomotor tone due to causes which may be varied, and many of them remain unknown.

This slide merely demonstrates an example of the study, to which Dr. Cordell referred, in which the arterial pressure following the onset of perfusion was definitely reduced. Still, during perfusion, this pressure tended gradually to increase, in spite of the total blood flow remaining constant. Of course, the total peripheral resistance concomitantly increased during this time.

The fact that the blood pressure did decline during perfusion is of concern, and I wonder if it would be appropriate to try to examine these data that have been presented today to see how they influence our selection of an optimal system of perfusion. I think the basic requirement of perfusion is provision of the tissues of the body with the necessary metabolic wants and needs, and it would seem that to accomplish that we must provide an ample flow of blood or "normal" blood flow to the capillaries of those tissues. The question is: Is it better to control the flow through the capillaries by perfusing at a theoretically given normal rate or by arterial or venous pressure levels, or is it better to perfuse according to the chemical nature of the blood returning to the machine?

We feel that there are ample data to demonstrate that the capillary blood flow is normal as long as the total body perfusion is in the theoretically normal range. Since vasomotor control and tone are so variable, it is better to perfuse at a given rate and disregard changes in pressure than it is to control the rate of perfusion on the basis of pressure levels alone.

DR. J. L. ANKENEY, Cleveland, Ohio.—We, too, have been interested in the effect of perfusion upon vascular resistance and have carried out a series of experiments in which arterial pressure and cardiac output (measured by a rotameter) were recorded and vascular resistance calculated before and after a 45-minute period of extracorporeal bypass. In all animals, hypotension followed perfusion and, in each instance, cardiac output was significantly reduced. In those animals perfused at 100 c.c./Kg./min. (high flow), there was no significant change in vascular resistance as a result of perfusion. However, in dogs perfused at 50 c.c./Kg./min. (low flow), the total vascular resistance was significantly reduced.

Therefore, we found hypotension following high flow perfusion is due to a decrease in cardiac output and not to a change in vascular resistance. Hypotension after low flow rates, however, is due not only to decreased cardiac output but also to a decrease in total body vascular resistance. Postperfusion transfusions return cardiac output and pressure to control levels. Therefore, we have found it efficacious to bring all patients off perfusion with a positive blood balance. As a result, hypotension postoperatively has not been a problem and vasodepressors have not been necessary.

DR. MERRILL P. SPENCER, Winston-Salem, N. C.—I find myself in considerable agreement with Dr. McGoon's remarks when he indicated that the peripheral resistance can be ignored if you use an adequate flow rate.

Our approach to this problem has been to examine the general total body response to perfusion. It is our plan, as I believe Dr. Kittle indicated, to study regional flow in animals, but for this particular presentation we confined ourselves to the total peripheral resistance.

Among the many factors which can influence peripheral resistance, we have the carotid sinus reflex and we have the agents which have been liberated from breakdown of the cells of the body as it is traumatized, to a greater or lesser extent, through the perfusion apparatus.

The carotid sinus reflex itself is a very basic mechanism, and seems to be a good thing to explain most of the results that we and others have shown. This reflex would predict the findings that Read and his co-workers have shown; namely, that as one increases the flow, the total pressure goes up, but it levels off, so that one reaches a level of pressure where there can be a great change in flow in the body with relatively small changes in pressure. This happens to be within the range of normal arterial pressure, and we find that the maintenance of a normal arterial pressure is not a good indication of whether or not the body tissues are adequately perfused. We should maintain a normal perfusion rate in preference to a normal pressure.

Factors involving the local changes must be studied. We know that the coronary bed and the cerebral bed require a normal arterial pressure in order to get an adequate flow. The brain seemingly has no prominent local mechanism to regulate its flow, so certainly it needs a pressure somewhere within normal range. As far as the rest of the body is concerned—the kidney, the liver, the muscle bed—they undoubtedly show the acidosis of low flow conditions and cause a great deal of trouble in the postoperative period.

We shall say in conclusion that we feel that the flow through the total body is extremely important, and this should be maintained at a high level. Certainly other factors should be monitored, such as arterial pressure and pH (to see whether or not we are getting any acidosis). We must find a way of correcting our pH readings readily and rapidly for CO_2 changes.

We believe that the oxygen tension is very important, particularly in the venous blood returning to the heart, but it is our opinion that the total body flow gives the key factor that must be monitored during perfusion.

LIPURIA AND LIPASEMIA AFTER THORACIC SURGICAL PROCEDURES

F. Price Cossman, M.D. (by invitation), Federico Adler, M.D. (by invitation), C. Frederick Kittle, M.D., and Leonard F. Peltier, M.D. (by invitation), Kansas City, Kan.

THE OCCURRENCE of an elevated serum lipase and the presence of urinary fat in certain diseases and after trauma, associated with operations and injuries, has been noted by several investigators.[11, 12, 28, 29] In some instances these findings have been interpreted as indicative of fat embolization.[4, 9, 18, 21] An elevated serum lipase and lipuria have been demonstrated to occur after fractures,[22] after various orthopedic and soft tissue procedures,[8, 20, 24] in patients with diabetic glomerulosclerosis,[13] and in acute pancreatitis.[15]

Robb-Smith[25] reviewed 789 accidents in which 125 deaths occurred. He was the first to emphasize the importance of large fat globules in the serum of patients dying with fat embolism, although this had been noted previously by others.[35, 36, 37]

Peltier[23] effectively demonstrated the value of a tourniquet in operations upon bone to prevent fat droplets from entering the systemic circulation. On the basis of experimental and clinical data he advised application of a tourniquet in operative procedures involving the bone in order to decrease fat embolism.

Bryans and Eiseman[3] studied 130 patients undergoing various surgical procedures. Sixty-seven of these had had operations involving the soft tissues. Fifty-one of these operations were classed as major procedures; 24 of the patients had postoperative fat globules in the serum. Sixteen were minor procedures; 3 patients had postoperative fat globules. In 37 patients undergoing orthopedic procedures, the incidence of fat globulinemia in 15 major operations was 66.6 per cent (10 patients) and in 22 minor operations was 22.7 per cent (5 patients). They concluded that fat globulinemia is correlated with the degree of operative trauma. In 5 dogs, they fractured the femur of each leg individually and then examined the serum for fat globules after each fracture. In each animal at least one examination showed fat globules in the

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serum, but in 9 of the 20 analyses no globules were noted. They believed that if the origin of the fat globules were from the fracture sites, a higher incidence of globules would be expected.

In an analysis of 75 orthopedic patients, Peltier and Lai[24] found 16 of them with a significantly elevated serum lipase. Twenty of these patients had had elective orthopedic procedures, 48 sustained fractures of one bone, and 7 sustained multiple fractures. No patient with a minor bone injury or with injuries limited to the soft tissue had an elevated serum lipase.

McKeown[19] studied the surgical specimens from 17 patients after lobectomy or pneumonectomy and the lung biopsies of 24 patients having mitral valvotomy. In 10 of the 17 resected lung specimens and in 4 of the 24 lung biopsies, she found fat emboli in the lung. In 2 of the patients, bone marrow emboli were found within the pulmonary vessels. She believed these to be incidental findings and of no clinical significance.

Schmidt[27] has reported a patient with atrial septal defect and anomalous pulmonary venous return who developed symptoms of embolism on the third postoperative day following an exploratory pericardiotomy. The patient died on the fifth postoperative day from bone marrow and fat embolism to the lungs.

Because of our interest in the problem of fat embolism, we should like to present our study of hyperlipasemia and lipuria following various types of thoracotomies, including those with extracorporeal circulation. A series of patients undergoing other surgical procedures is used for comparison. The data include 110 patients, of whom 38 had thoracotomy, 19 utilizing extracorporeal circulation; 32 with either laparotomy or major surgical procedures on soft tissues; and 40 with operative procedures involving fresh skeletal trauma.

METHODS

Samples of the patients' blood and urine were obtained on the day prior to operation and on succeeding days up to the eighth postoperative day. Immediately after obtaining the blood it was transferred to centrifuge tubes, allowed to clot, and centrifuged with subsequent removal of the serum. The urine in most instances was collected from patients after insertion of an indwelling catheter. Samples were collected in volumetric flasks previously washed carefully to remove all traces of fatty substances.

Serum lipase was determined by the method of Cherry and Crandall,[5] as modified by Comfort and Osterberg.[6] This consists essentially of incubating 1.0 ml. of serum with a buffered olive oil emulsion at 37° C. for 24 hours. The free fatty acids released by hydrolysis are then titrated to an end point with 0.5N sodium hydroxide. Results are reported in milliliters of 0.5N sodium hydroxide. The mean serum lipase by this method in our laboratory in 100 normal individuals was 0.37, with a standard deviation of 0.26.

Lipuria was measured by the method of Scuderi.[31] The meniscus of urine in the volumetric flask was skimmed with a 3 mm. platinum loop and its contents smeared on a glass slide. After the slide had been permitted to dry, it was covered with several drops of a saturated solution of Sudan III and 70 per

TABLE I. PATIENTS UNDERGOING THORACOTOMY WITH EXTRACORPOREAL CIRCULATION*

PATIENT	AGE (YEARS)	HEIGHT (INCHES)	WEIGHT (POUNDS)	AREA ($M.^2$)	DIAGNOSIS	PROCEDURE	INCISION	DURATION OF BYPASS (MIN.)
PV	13	50	52.2	0.92	Trilogy of Fallot	Pulmonary valvotomy	Sternal splitting	55
DA	7	49	44.6	0.85	V. S. D.	Closure V. S. D.	Sternal splitting	13
MD	47	61.5	136.4	1.61	A. S.	Aortic valvotomy	Sternal splitting	25
LG	37	67.5	159.9	1.84	A. S. D.	Closure A. S. D.	Transverse thoracotomy	36
EH	13	62	105.5	1.45	V. S. D.	Closure V. S. D.	Sternal splitting	44
JM	5	44	40.6	0.75	V. S. D.	Closure V. S. D.	Sternal splitting	19
DG	5	42	37.2	0.70	V. S. D.	Closure V. S. D.	Sternal splitting	15
JW	27	65	106.3	1.51	M. I.	Mitral repair	Transverse thoracotomy	43
JT	3	33.8	23.1	0.49	V. S. D.	Closure V. S. D.	Sternal splitting	22
PM	13	60.5	85.0	1.30	P. S.	Pulmonary valvotomy	Sternal splitting	55
JD	8	47.5	49.3	0.87	V. S. D.	Closure V. S. D.	Sternal splitting	47
JR	12	58	104.8	1.38	A. S.	Aortic valvotomy	Sternal splitting	21
JM	5	44	40.6	0.75	V. S. D.	Closure A. S. D.	Sternal splitting	19
PP	25	71.5	184.6	2.03	A. S.	Aortic valvotomy	Sternal splitting	40
KD	6	43	35.8	0.70	A. S. D.	Closure A. S. D.	Sternal splitting	37
JJ	7	45.2	40.7	0.77	A. S.	Aortic valvotomy	Sternal splitting	21
JC	6	47	49.3	0.86	P. S.	Pulmonary valvotomy	Sternal splitting	39
MM	9	51	54.4	0.95	A. S.	Aortic valvotomy	Sternal splitting	32
WR	53	69.3	145.9	1.81	A. S.	Aortic valvotomy	Sternal splitting	33

**Legend:* V.S.D. = ventricular septal defect; A.S. = aortic stenosis; A.S.D. = atrial septal defect; M.I. = mitral insufficiency; P.S. = pulmonary stenosis.

cent alcohol. The slide was covered with a cover slip and immediately examined microscopically. The urine also was examined microscopically by the method of Adler, Peltier, and Lai.[1] This consists of a staining technique utilizing Nile blue sulfate as a selective dye. Five drops of this staining solution are layered on the surface of urine in the volumetric flask. After 2 minutes, five drops of ether are added. Following evaporation of the ether, the walls of the flask are examined. If fat globules are present, small drops of pink-to-red color will be precipitated on the walls of the flask above the meniscus.

RESULTS

In the 19 patients who had a thoracotomy with extracorporeal circulation, 9 were males, 10 were females, and their average age was 15.9 years. In 17 patients, a sternal splitting incision was used, and, in 2, an intercostal incision (Table I). Seven patients had a ventricular septal defect, 6 aortic stenosis, 2 atrial septal defect, 2 pulmonary stenosis, 1 mitral insufficiency, and 1 tetralogy of Fallot. Preoperatively (Table II), the mean serum lipase in this group was 0.40 ml. with a standard deviation of 0.20; 3 patients had urine positive

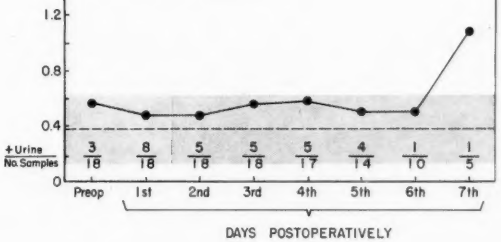

Fig. 1.

for fat. Postoperatively, the mean value for serum lipase on the first postoperative day was 0.48 with a standard deviation of 0.28, on the second day 0.65 with a standard deviation of 0.71, on the third day 0.95 with a standard deviation of 0.70, on the fourth day 0.98 with a standard deviation of 0.71, and on the fifth day 0.92 with a standard deviation of 0.67. Lipuria was found in 9 of the 17 patients on the first postoperative day, 8 of 17 patients on the second day, 9 of 18 patients on the third day, 8 of 17 patients on the fourth day, and 4 of 16 patients on the fifth day.

All patients undergoing thoracotomy without extracorporeal circulation were adults. This group was composed of 7 males and 12 females. Preoperatively (Table III), mean serum lipase was 0.56 ml. (standard deviation 0.47). Lipuria was found in 2 patients before operation. The mean value for serum lipase was 0.47 ml. (standard deviation 0.32) on the first postoperative day, 0.47 ml. (standard deviation 0.33) on the second day, 0.56 ml. (standard deviation 0.41) on the third day, 0.58 ml. (standard deviation 0.57) on the

TABLE II. LIPASEMIA AND LIPURIA IN PATIENTS IN WHOM EXTRACORPOREAL CIRCULATION WAS USED*

PATIENT	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
PV	0.76	–	1.04	+		–	1.55	–	2.73	+	2.95	–	2.55	–				
DA				++		+	0.95	+	1.15	–		–						
MO			0.85	–	2.43	+	2.81	+		+		+		+		+		
LG				+	0.28	+	1.60	+	1.35	+	0.89	+	2.79	+	2.56	+		
EH	0.31			+		+	0.17	+	0.51	+		+	0.71	+	0.43	+		
JM	0.33			+		+	1.08	+	0.29	+	0.60	–		–				
DG	0.37		0.07	–	2.19	–	1.62	–	1.62	–	1.27	–	1.17	–				
JW	0.49		0.22	+	0.66		1.25	+	2.31	+	1.47		1.09	+	2.56	+	2.74	+
JT	0.10		0.49		0.69		0.92		0.58		0.32							
PM			0.37	+	0.26	–		–	0.22	–	0.69	–	0.61	–	0.22	–		
JD	0.38					–		–		+	0.75	–	0.81	–	0.40	–	0.47	–
JR	0.42	±	0.23	–	0.53	–	0.91	–	1.14	–	0.69	–	0.42	–	0.27	–		
JM	0.28	±	0.91	+	0.20	–	0.30	+	0.36	–	0.43	–	0.47	–				
PP	0.93	+	0.52	–	0.45	–	0.45	+	0.38	–	0.09	–	0.43	–	0.44	–		
KD	0.27	–	0.38	–	0.00	+	0.00	–	0.45	–	0.10	–	0.23	–	0.16	–		
JJ	0.40	–	0.52	±	0.48	±	0.58	+	1.16	+	1.34	+	1.26	+				
JC	0.34	–	0.47	–	0.20	–	0.25	–	0.58	–	1.00	–	1.16	–	1.40	–		
MM	0.14	–	0.12	–	0.15	–	0.26	–	0.48	–	0.74	–	1.31	–	1.94	–	1.31	–
WR	0.47	–	0.49	–	0.62	±	1.50	–	1.34		1.40							
Mean	0.40		0.48		0.65		0.95		0.98		0.92		1.07		1.04		1.50	
S. D.	0.20		0.28		0.71		0.70		0.71		0.67		0.74		0.94		0.97	

*B = blood; U = urine.

TABLE III. LIPASEMIA AND LIPURIA POSTOPERATIVELY IN PATIENTS UNDERGOING THORACOTOMIES WITHOUT EXTRACORPOREAL CIRCULATION*

	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
PATIENT	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
WF	0.08	±	0.12	–	0.16	–	0.28	–	0.14	–	0.36	–	0.73	–				
NS	0.85	–	0.34	±	0.38	++	0.24	–	0.38	–	0.38	–	0.40	–	0.44	–	0.22	–
HB	0.67	–	0.52	–	0.44	–	0.50	–	0.48	–	0.41	–						
LM	0.20	–	0.18	–	0.52	–	0.11	+	0.15	+	0.15	+	0.18	–				
CM	0.32	–	1.02	+	1.23	+	1.49	+	1.97	+								
AS	0.36	–	0.33	++	0.37	–	0.37	+	0.21	–	0.31	–	0.33	–				
DM	0.22	–	0.31	+	0.21	–	0.24	–	0.19	–	0.17	–	0.22	–				
MK	0.37	–	0.50	–	0.34	–	1.27	–	0.49	–	0.80	–						
JW	0.49	–	0.22	±	0.66	±	1.25	+	2.31	+	1.47	+	1.09	+	2.56	+	2.74	+
EJ	0.37	–	0.64	–	0.30	–	0.53	±	0.99	±	0.69	±						
ME	2.31	–	1.27	±	1.09	–	0.78	–	0.68	–	0.69	±						
GN	0.50	–	0.34	–	0.24	–	0.31	–	0.52	–	0.28	–						
GS	0.54	–	0.56	–	0.31	–	0.37	–	0.20	–	0.25	–	0.36	–				
IG	0.87	–	0.54	–	0.77	–	0.56	–	0.54	–	0.76	–	0.77	–	1.08	–		
LH	0.80	–	1.08	–	1.05	±	1.11	–	0.60	±								
MM	0.69	–	0.21	±	0.16	±	0.44	–	0.49									
JS	0.29	–	0.24	±	0.22	–	0.22	–	0.31		0.46	–	0.51	–	0.24	–		
MR	0.32	+	0.42	–	0.33	–	0.40	–	0.29		0.27		0.44					
LM	0.31		0.06		0.09		0.11		0.15		0.05							
Mean	0.56		0.47		0.47		0.56		0.58		0.50		0.50		1.08			
S.D.	0.47		0.32		0.33		0.41		0.57		0.33							

*B = blood; U = urine.

fourth day, and 0.50 ml. (standard deviation 0.33) on the fifth day. Lipuria was found in 8 of 18 patients on the first postoperative day, 5 of 18 patients on the second day, 5 of 18 patients on the third day, 5 of 17 patients on the fourth day, and 4 of 14 patients on the fifth day.

Thirty-two patients undergoing laparotomy (Table IV) were studied for serum lipase levels. These may be considered as having major soft tissue trauma. Preoperatively, the mean serum lipase was 0.59 ml. with a standard

TABLE IV. LIPASEMIA IN PATIENTS AFTER ABDOMINAL OPERATIONS AND OTHER PROCEDURES

NAME	PREOP.	DAYS POSTOPERATIVELY 1ST	2ND	3RD	4TH	5TH	6TH	PROCEDURE
TE	0.60	0.69	0.56	0.78	1.07	1.19	2.02	Gastrectomy
ET	0.69	0.54	0.67	0.31	0.14	0.36	0.73	A-P resection
JC	0.24	0.33	0.14	0.08	0.10	0.05		Gastrectomy
LE	0.68	0.43	0.53	0.43	0.49			Cholecystectomy
HK	0.41	0.16	0.09	0.18	0.13	0.40		Bilateral herniorrhaphy
JB	0.17	0.27	0.00	0.12	0.13	0.14		Gastrectomy
RG	0.98	0.26	0.29	0.14	0.94	0.23		Cholecystectomy
BR	0.47	0.17	0.04	0.46	0.75	0.83		Colectomy
EB	0.27	0.20	0.54	0.93	0.90	1.15		Cholecystectomy
CR	1.49	1.54	0.33	1.07	1.14	1.11		Exploratory laparotomy
KM	0.47	0.57	2.53	1.02	1.20	2.04		Splenectomy
AM	0.11	0.09	0.40	0.68	1.20	2.71		Cholecystectomy
RB	1.64	1.05	0.09	0.09	0.22	0.33		Exploratory laparotomy
CO	0.73	0.59	0.25	0.51	0.63	1.29		Colectomy
RW	0.88	0.95	2.17	2.14	1.46			Colectomy
DS	0.55	0.26	0.23	0.72	0.39			Splenectomy
ND	0.29	0.08	0.62	0.30	0.29	0.46		Colectomy
GP	0.38	0.42	0.00	0.15	0.29	0.73		Bilateral herniorrhaphy
KM	0.23	0.04	0.18	0.14	0.30	0.30		Splenectomy
AR	0.68	0.86	0.60	0.90	0.82	1.07		Gastrectomy
EE	0.57	0.23	0.05	0.19	0.61			Cholecystectomy
BT	0.36	0.38	0.32	0.52	0.50			Colostomy
RW	0.80	0.46	0.14	0.00	0.03	0.34		Splenectomy
LS	0.10	0.31	0.03	0.00	0.00	0.00		Gastrojejunostomy
HS	1.11	0.45	0.60	0.81	0.82	0.91		Resection of jejunum
AH	0.26	0.10	0.04	0.86	0.00			Cholecystectomy
RD	0.33	0.13	0.00	0.09	0.40	0.13		Pelvic floor repair
OG	0.47	5.91	1.24	1.07	1.05			Exploratory laparotomy
DK	1.63	1.45	0.83	0.87	0.82	0.86		Cholecystojejunostomy
CR	0.43	0.35	0.31	1.32	1.99	2.49	1.57	Gastrojejunostomy
CH	0.13	0.15	0.17	0.16	0.09	0.07		Lumbar sympathectomy
JB	0.76	0.08	0.00	0.42	0.38	0.31		Gastrectomy
Mean	0.59	0.64	0.44	0.54	0.61	0.78		
S.D.	0.40	1.03	0.57	0.47	0.45	0.72		

deviation of 0.40. The mean serum lipase level was 0.64 ml. with a standard deviation of 1.03 on the first postoperative day, 0.44 ml. with a standard deviation of 0.57 on the second day, 0.54 ml. with a standard deviation of 0.47 on the third day, 0.61 ml. with a standard deviation of 0.45 on the fourth day, and 0.78 ml. with a standard deviation of 0.72 on the fifth day after operation.

Forty patients who had orthopedic operations with bone trauma had a mean serum lipase of 0.50 with a standard deviation of 0.32 preoperatively (Table V). Lipuria was found preoperatively in 10 of these patients. The

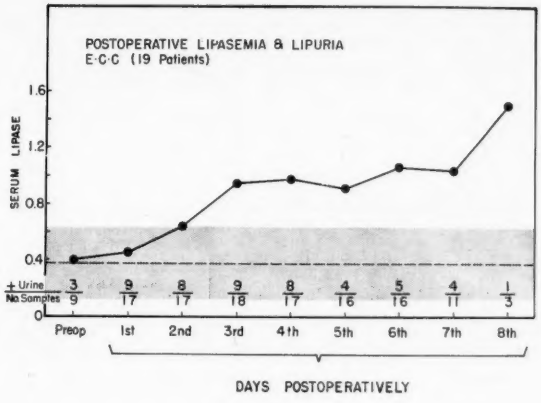

Fig. 2.

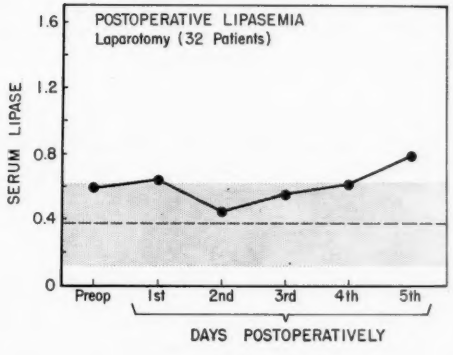

Fig. 3.

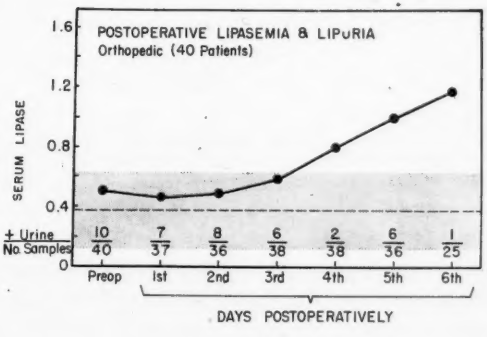

Fig. 4.

TABLE V. LIPASEMIA ASSOCIATED WITH TRAUMA TO BONE*

	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
PATIENT	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
IC	0.51	–	0.94	–	0.27	+	0.84	–	0.75	–	1.09	–	0.57	–				
CW	0.75	–	0.24	–	0.46	–	0.69	–	0.81	–	0.85	–	0.70	–				
FM	0.36	–	0.44	–	0.62	–	2.07	–	2.23	–	3.79	–	3.20	–	3.06		228	
GD	1.24	–	1.19	–	0.90	–	0.65	–	1.05	–	0.70	–	1.21	–				
RC	1.15	–	0.73	–	0.77	–	0.72	–	1.30	–	1.68	–	1.71	–				
AM	0.00	–	0.00	+	0.26	–	0.08	–	0.03	–	0.16	–						
KM	0.59	–	0.39	–	0.04	–	0.17	–	0.23	–	0.73	–						
MT	0.41	–	0.52	–	0.52	–	0.66	–	0.60	–	0.48	–	0.45	–				
JU	0.00	–	0.29	–	0.36	–	0.32	–	0.38	–	0.59	–	0.51	–				
EW	0.58	+	0.22	–	0.45	++	0.37	–	0.56	–	1.07	+						
JA	0.29	++	0.01	–	1.10	–	0.09	–	0.00	–								
MH	0.28	–	0.22	–	0.14	–	0.40	–	0.04	–	0.13	–	0.42	–				
MM	0.55	++	0.67	–	0.27	–	0.53	–	1.07	–	1.54	–	2.73	–				
SZ	1.24	–	1.38	–	1.33	–	1.29	–	1.79	–	1.11	–	1.32	–				
LC	0.16	–	1.14		0.31	+	0.31	–	0.45	–	0.37	–	0.72					
FW	0.90	–	0.73	–	0.78		1.00	–	1.21	–	1.99	–	2.31					
LB	0.26	–	0.31		0.51		0.51		0.52		0.58		0.57					
MJ	0.56	+	0.49		0.59	–	0.55	–	0.36	–	0.59	+	0.51	–				
EE	0.12	++	0.22	–	0.38	+	0.84	+	0.46									
CS	0.28	–	0.35	+	0.35	+	0.21	–	0.18	–	0.55	+	0.77	–	0.85	–	1.22	
LJ	0.45	++	0.37	–	0.21	+	0.29	–	0.28	+	0.32	+	0.43					
CT	0.08	–	0.32	–	0.47	–	0.19	–	1.31	–	1.91	–	2.31	–				
EM	0.69	–	0.79	–	0.40	–	0.98	–	1.09	–	1.27	–						
JK	0.71	–	1.35	+	0.80	–	0.54	+	2.44	–	3.44	–	3.62	–				
CW	0.34	++	0.13	–	0.20	–	0.28	++	0.75	++	0.58	+	0.68	–				
AC	0.59	–	0.40	–	0.33	–	0.39	–	0.81	–	0.46	–						
OC	1.01	–	0.60	–	0.57		0.78	–	1.13	–	1.67							
JA	0.52	–	0.12	–	0.24	+	0.26	–	0.35	–	0.51	–						
LM	0.41	–	0.50	–	0.79	–	0.78	+	0.87	–	1.21	–	1.27	–				
JB	0.90	–	0.47	+	0.45	–	0.56	–	0.65	–	1.31	–	0.52	–				
DF	0.13	+	0.30	–	0.87	–	1.36	–	1.77	–	1.10	–	0.97					
CT	0.19	+	0.11	+	0.31	–	0.50	+	1.30	–	1.35	–	1.27	–				
DW	0.70	+	0.44	–	0.34	+	0.19	+	0.17	–	0.22		0.33	+				
AB	0.61	–	0.44	–	0.54		0.46	–	0.60	–	1.01	–	1.03	–				
EE	0.19	–	0.41	+	0.14	–	0.30	–	0.63	–	0.63	+	0.74	–				
CC	0.48	–	0.68	–	0.50	–	1.00	–	0.74	–	0.83	–	1.04	–				
JM	0.40	–	0.19	–	0.38	–	0.51	–	1.00	–	0.68	–						
MC	0.91	–	0.45	–	0.56	–	0.54	–	0.72	–	0.90	–	0.92	–				
MH	0.21	–	0.23	+	0.30	–	0.34		0.42	–	0.36	–	0.44	–				
OG	0.40	–	0.48	–	0.62	–	0.97	–	0.77	–	1.27	–	1.63	–				
Mean	0.50		0.46		0.48		0.59		0.80		1.00		1.16					
S.D.	0.32		0.32		0.26		0.39		0.56		0.77		0.85					

*B = blood; U = urine.

mean serum lipase was 0.46 ml. (standard deviation 0.32) on the first postoperative day, 0.48 ml. (standard deviation 0.26) on the second day, 0.59 ml. (standard deviation 0.39) on the third day, 0.80 ml. (standard deviation 0.57) on the fourth day, and 1.00 ml. (standard deviation 0.77) on the fifth day after operation.

DISCUSSION

Parenchymatous embolism is an ubiquitous and protean manifestation of trauma. The association of such embolism with cardiac or thoracic operations may seem tenuous but deserves consideration. This study of lipasemia and lipuria was carried out because of our interest and the observation that fat embolism has been noted in patients who die soon after cardiac operations.[29] In our hands, elevation of the serum lipase and demonstration of lipuria have been the most valuable laboratory methods in the diagnosis of fat emboli in surgical patients.

In our group of patients, the incidence of lipuria was widespread and without significance. It appears that there is a marked elevation in the serum lipase levels, reaching the peak after the third postoperative day, in patients with thoracotomy and extracorporeal circulation and in those with trauma to the bone.

The factor of bone trauma must be considered in both groups since, in all but 2 of the 19 patients with thoracotomy and extracorporeal circulation, a sternal splitting incision was made. However, in the two exceptions, elevations of the serum lipase levels also occurred. This attracts attention to other possibilities.

Haymaker[14] and Gersh[10] and their associates have shown that fat embolism appears in patients and animals in whom there has been a sudden drop (by decompression) in the partial pressure of nitrogen in the blood. This was believed to be due to rupture of fat cells by bubbles of escaping nitrogen dissolved in the fat under previous ambient pressure. We have found that by suddenly shifting the composition of the atmosphere from 95 per cent nitrogen and 5 per cent oxygen or from 80 per cent nitrogen and 20 per cent oxygen to 100 per cent oxygen, rats, in a period of 10 minutes, developed pulmonary fat embolism.[7] It appears feasible, therefore, that sudden changes in local fatty tissue pressure of nitrogen may result in the phenomena described by Gersh and his co-workers.

The source of fat in both circumstances may be local trauma to fat cells in the sternum or diffuse trauma to fat cells because of the rapid variation in pN_2. Swank[34] and Lehman[16] and others have shown experimentally that fat globules in the circulating blood as a metabolic lipemia may agglomerate to form fat emboli. Recently we have repeated their experiments but have failed to confirm their findings. On this basis, we believe that the conclusion of Scott and his co-workers,[30] regarding the source of embolic fat from blood lipids, is unwarranted.

^{a}B = blood; U = urine.

Lipase is known to be present in or secreted by the stomach, pancreas, liver, lung, and leukocytes, as well as many other organs and tissues.[8, 32] In these patients we believe the source of the elevated lipase most probably to be the lung. Lipase from other organs and tissues is not secreted in sufficient quantity to elevate blood levels, while lung lipase is secreted in response to the presence of emboli of neutral fat to the lung.[21] Under normal circumstances there is no relationship between metabolic or alimentary lipemia and an elevated serum lipase. However, in patients with chronic hyperlipemia the serum lipase may be elevated.[32] LeVeen and his associates[17] recently have shown that no appreciable change in blood lipid levels occurs in patients postoperatively.

In hyperlipasemia after extracorporeal circulation, some consideration should be given to the lipase changes after administration of heparin. Lipase activity can be detected in the plasma shortly after intravenous injection of heparin.[33] The addition of heparin to normal plasma in vitro does not initiate lipase action in the plasma or a lipid emulsion added to normal plasma which contains heparin is not cleared.[2] These observations suggest that the lipase, or some component necessary for its action, is released into the plasma by the injected heparin from some immediately accessible site. It has been suggested that the essential component is distributed generally in the walls of blood vessels in the body.[26] In our patients the failure of the serum lipase to become elevated until the fifth day minimizes the importance of this factor.

CONCLUSIONS

1. Determinations of serum lipase and urinary fat have been made in 110 patients undergoing a variety of surgical procedures. Nineteen had thoracotomy using extracorporeal circulation; 19 had thoracotomy alone; 32 had laparotomy for major surgical procedures involving soft tissue; and 40 had orthopedic operations with skeletal trauma.

2. Lipuria was noted occasionally in patients both preoperatively and postoperatively; because of its sporadic occurrence, no significance is ascribed to it.

3. Serum lipase was significantly elevated in patients with thoracotomy, most of whom had had sternal splitting incisions, and in patients undergoing orthopedic operations with bone trauma.

4. Possible explanations for this hyperlipasemia are suggested.

5. No clinical significance of the elevated serum lipase or lipuria has been noted.

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Discussion

DR. LEWIS H. BOSHER, Richmond, Va.—Dr. William H. Scott 2 years ago called attention to the importance of fat mobilization during extracorporeal circulation, and, as a result of his work, we asked Dr. John Forbes in our Biochemical Department to make some fat studies for us.

On seven prolonged perfusions, Dr. Forbes studied the cholesterol and neutral fats in patients about 5 minutes after initiating the perfusion, and at the end of perfusion [slide]—these figures represent the average of seven prolonged perfusions, averaging 1 hour and 54 minutes, and in the first row you have the values seen for total cholesterol and neutral fats in milligrams per cent. At the end of the perfusion there is no change in these values. We concluded there was no evidence for mobilization of fat during the perfusion. In addition, Dr. Forbes centrifuged the serum at 20,000 g; this technique also failed to show any change in the values.

It's hard, I think, to interpret these figures, and I don't know how they fit into the results that have just been reported, but I present them for what they are worth.

DR. JAMES V. MALONEY, Los Angeles, Calif.—I particularly enjoyed this paper by Dr. Cossman, Dr. Adler, and Dr. Kittle for two reasons. First, the paper has the same scientific exactitude as the paper they presented 2 years ago; and now they are showing, perhaps, that similar endogenous materials may exist. Second, I enjoyed it because we can support it with some experiments from our laboratory.

Drs. Fonkalsrud, Miller, and Latta in our laboratory studied the autopsy material in 40 patients who had undergone surgical procedures with the use of the pump-oxygenator and who died in our hospital during the past 5 years. Interestingly enough, in between 55 and 80 per cent of the cases, extensive fat embolism could be found, depending on which organ was examined. We were at that time quite excited by the clinical significance of these findings until we ran control observations. Much to our surprise, 63 per cent of the routine autopsy specimens in the surgical service were found to have extensive fat embolism. Strangely enough, the patients who come from medical wards rarely have fat embolism demonstrated in their tissues at autopsy.

We certainly would agree with Dr. Cossman's concluding statement, that we are much in the dark as to the exact clinical significance of these findings. Nevertheless, it certainly does appear that there are extensive changes in the lipid system of the body under extracorporeal circulation.

DR. KITTLE (Closing).—I wish to thank Dr. Bosher and Dr. Maloney for their remarks.

I can't explain the discrepancy between data presented by Dr. Bosher and our finding of hyperlipasemia. Unquestionably in many patients there is a significantly and definitely elevated serum lipase. What this means, I think, yet remains to be unraveled.

The finding of Dr. Maloney about fat emboli in autopsy material correlates very well with a previous study by Vance which shows a high incidence of microscopic fat emboli in routine autopsies.

THE SURGICAL TREATMENT OF EMPHYSEMATOUS BLEBS AND LOCALIZED VESICULAR AND BULLOUS EMPHYSEMA

Analysis of 50 Cases

James M. Head, M.D. (by invitation), Louis R. Head, M.D. (by invitation), Theodore R. Hudson, M.D., and Jerome R. Head, M.D., Chicago, Ill.*

THE SURGICAL treatment of emphysema is one of the most recent, most difficult, and most challenging fields in thoracic surgery. The numerous publications in the recent literature[1-19] attest to the newness of this therapeutic approach. It is difficult chiefly in its indications and challenging because the incidence of this crippling and eventually fatal disease seems to be increasing as rapidly as is that of bronchogenic carcinoma.

The present paper is a report of the immediate and late results in 31 patients operated upon for emphysematous blebs and 19 patients operated upon for localized vesicular and bullous emphysema. It is therefore divided into two parts.

EMPHYSEMATOUS BLEBS

Discussion.—Emphysematous blebs (Fig. 1) are blisters beneath the visceral pleura. They are to be distinguished from lung cysts, which are congenital, and from localized areas of extreme vesicular and bullous emphysema.[20, 21] The latter result from the breakdown of interalveolar septa. The large blebs (Fig. 2) with which we are to deal are probably of different etiology from the small apical blebs which so frequently cause spontaneous pneumothorax. The latter are probably caused by the apical scarring resulting from the usual apical deposits of the primary tuberculous infection. The former are usually associated with pulmonary emphysema, although as Laennec[22] pointed out, they may develop in otherwise healthy lungs.

On their outer surface these large blebs are covered with a thin layer of visceral pleura. When viewed from within with the thoracoscope during life, the lung surface has on it many alveolar openings which open during expiration and close during inspiration.[23, 24] This seemingly paradoxical phenomenon explains why they become distended after bouts of coughing and why, over the years, they increase steadily in size.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

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Blebs are usually multiple and bilateral, but may be single and unilateral. They may be truly gigantic (Fig. 3) and occupy most of the space in one or both pleural cavities. Korol,[25] Peabody, Katz, and Davis,[26] and West and Van Schoonhoven[27] have demonstrated that they predispose to bronchogenic carcinoma (Fig. 4). If they become infected so that fluid forms in them, the alveloar openings into them are closed, the air is absorbed, and they disappear.[28]

The surgical indications for the removal of large emphysematous blebs are obvious. Not only do they collapse the functioning lung in the same manner as does spontaneous pneumothorax, but they also tend to enlarge, and they predispose to carcinoma. In 1943 we first operated upon a man who had multiple large blebs at the apices of both lungs. After the operation, persistent air leaks

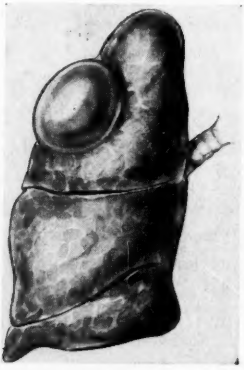


Fig. 1.—Schematic representation of an emphysematous bleb lying within the right upper lobe. Such blebs are to be distinguished from congenital lung cysts and from localized areas of extreme vesicular and bullous emphysema.

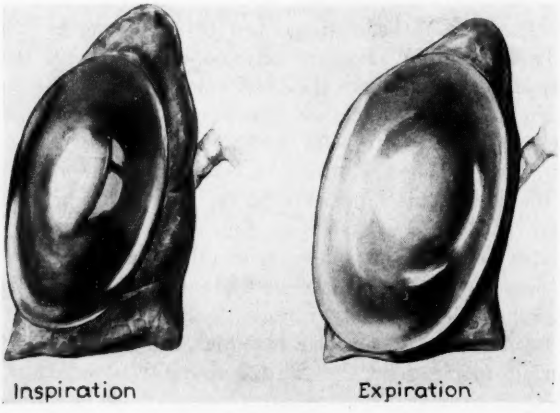


Fig. 2.—These large emphysematous blebs are covered with a thin layer of visceral pleura. The inner lung surface has on it many alveolar openings which open on expiration and close on inspiration. This paradoxical phenomenon causes them to enlarge during the expiratory phase of the cycle (coughing). During the inspiratory phase of the cycle, they tend to remain enlarged and distended for the pressure within them is much greater than the negative intrapleural pressure that occurs during inspiration. This explains why they become so distended after bouts of coughing and why, over the years, they increase steadily in size.

made it difficult to re-expand the lung and the patient almost died of retained secretions. He recovered, however, and his vital capacity was increased from 1,200 c.c. to 1,800 c.c.

In the early 1940's, at about the same time that the aforementioned patient was seen, we were using Monaldi's intracavitary suction to close tuberculous excavations. It occurred to us that this procedure might prove a simple and safe way of closing blebs. It did, and in 1948 we reported before this Society 8 cases in which this had been used successfully.[24] Today we believe

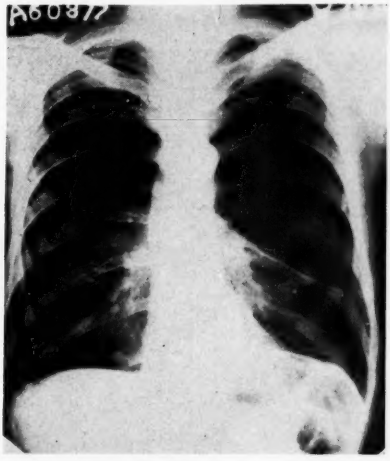


Fig. 3.—Roentgenogram which shows bilateral, multiple gigantic blebs which occupy most of both pleural cavities.

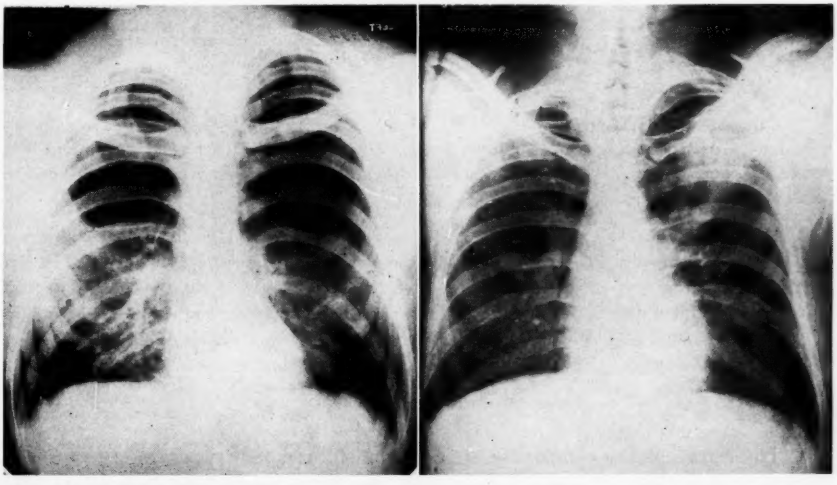


Fig. 4.—Roentgenograms of a 36-year-old white man who developed a bronchogenic carcinoma at the site of a previous bleb collapsed by Monaldi suction 2 years earlier.

that the open operation is preferable in all patients, save those who are extremely feeble and dyspneic, and perhaps even in these patients with the aid of the mechanical respirator. In most cases the blebs are multiple and today the refined techniques of open operation, the improvements in postoperative bronchial toilet, and the use of tracheostomy and the mechanical respirator have made the open operation very safe.

We have divided the cases of emphysematous blebs into two groups: the first, those in which, apart from the blebs, the lungs are normal, and the second, those in which they are complicated by an underlying generalized emphysema.

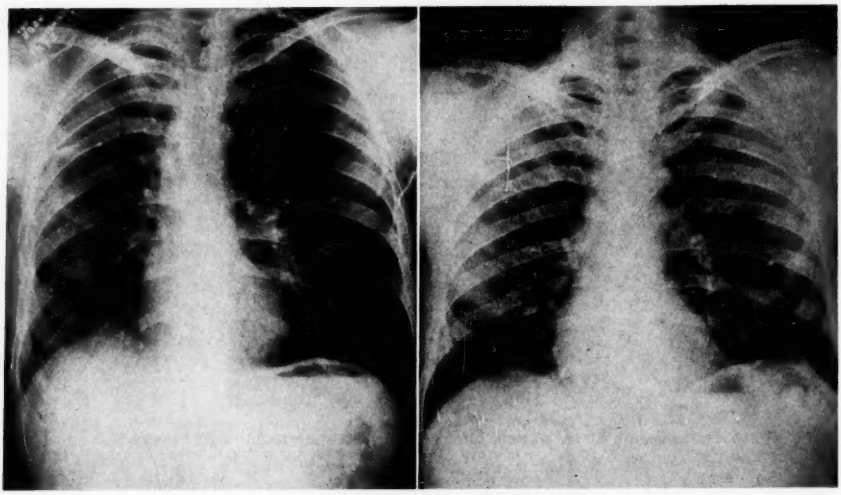


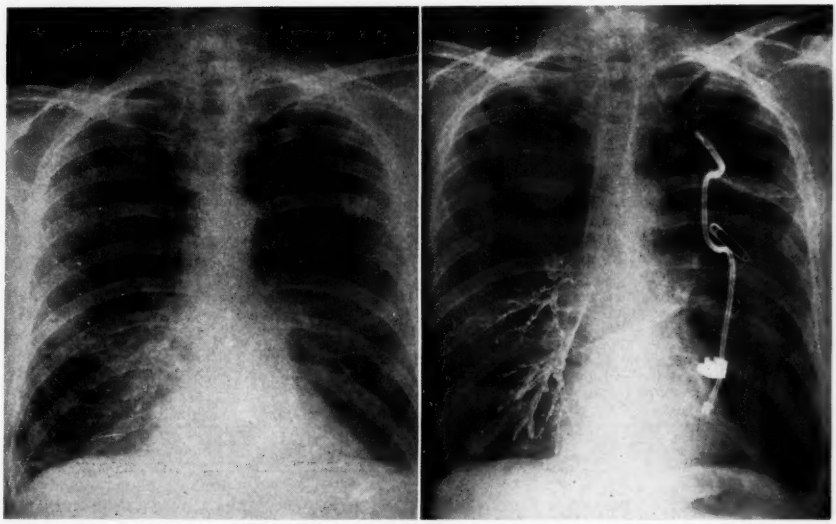
Fig. 5.—Case 1. Pre- and postoperative x-ray studies of a patient with blebs on normal lungs. After a second operation he had normal respiratory function.

Case Reports

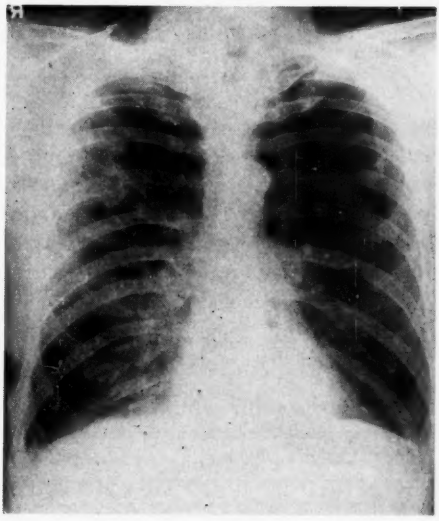
CASE 1.—B. S.; CWMH 389270. Fig. 5 shows the pre- and postoperative roentgenograms of a patient with blebs on normal lungs. Before the first operation the patient was markedly short of breath. Since the second operation, which was performed in 1954, he has had normal respiratory function.

CASE 2.—H. S.; CWMH 310423. Fig. 6 shows the pre- and postoperative roentgenograms of a patient with bilateral giant blebs complicated by generalized emphysema. Prior to the operation he was completely incapacitated, even dressing and shaving were too great a tax on his breathing. He could not tolerate respiratory function studies. After the operations, although still dyspneic on moderate exertion, he was sufficiently improved to be able to return to work. However, his dyspnea became gradually worse. At the end of 3 years he was again forced to stop work and 4 years after the operation he died of cor pulmonale.

These typical cases illustrate the essential difference between the two groups. In the uncomplicated cases, removal of the blebs gives both immediate and



A. *B.*



C.

Fig. 6.—Case 2. Pre- and postoperative roentgenograms of a patient with bilateral giant blebs complicated by emphysema. The bleb on the left was collapsed by Monaldi suction. The bleb on the right was resected. The patient died 4 years later of cor pulmonale. He had been working for 3 years prior to his death.

permanent relief. In those complicated by emphysema, the patients are greatly relieved immediately, but the emphysema always progresses and they die of right heart failure.

Operative Mortality and Type of Surgery.—Of the 31 patients operated upon for emphysematous blebs 3 have been lost to follow-up. Sixteen (57 per cent) of the remaining 28 patients (Table I) had blebs on underlying normal lungs, while 12 (43 per cent) had blebs complicated by pulmonary emphysema.

TABLE I. OPERATIVE MORTALITY AND TYPE OF SURGERY IN 28 PATIENTS OPERATED UPON FOR EMPHYSEMATOUS BLEBS

	NO. OF CASES	OPERATIVE MORTALITY	TYPE OF OPERATION		
			MONALDI	MONALDI + RESECTION	RESECTION
Uncomplicated by emphysema	16 (57%)	0 (0%)	4 (25%)	2 (12.5%)	10 (62.5%)
Complicated by emphysema	12 (43%)	0 (0%)	7 (58%)	1 (8%)	4 (34%)
Totals	28 (100%)	0 (0%)	11 (39%)	3 (11%)	14 (50%)

The operative mortality in this group of cases was zero.

Of the 16 patients with pure blebs, 4 (25 per cent) were treated with Monaldi suction, 2 (12.5 per cent) were treated with Monaldi suction plus resection, and 10 (62.5 per cent) were treated by resection alone.

Seven (58 per cent) of the patients with the complication of emphysema were treated with Monaldi suction, 1 (8 per cent) was treated with Monaldi suction plus resection, and 4 (34 per cent) were treated with resection alone.

Results and Long-Term Follow-Up.—All of the patients operated upon for pure emphysematous blebs (Table II) noted excellent immediate results. Only 2 (12 per cent) of these patients are recorded as having poor late results. One of the latter has been followed only for 2 months so that it is too early to determine the late result. However, we have every reason to believe that this patient will have an excellent long-term survival. The second patient died at the end of 2 years from a bronchogenic carcinoma which had arisen at the sit of a previous bleb collapsed by Monaldi suction. The patient was asymptomatic with regard to his initial disease at the time of death.

TABLE II. RESULTS AND DURATION OF FOLLOW-UP IN 16 CASES OF BLEBS UNCOMPLICATED BY EMPHYSEMA

IMMEDIATE RESULT		LATE RESULT		DURATION OF FOLLOW-UP						OVER-ALL RESULT	
GOOD	POOR	GOOD	POOR	2 MO.	1-2 YR.	2-4 YR.	8-10 YR.	12 YR.	TOTAL	EXCELL.	POOR
16 (100%)	0 (0%)	14 (88%)	2 (12%)	1 (6.25%)	6 (37.5%)	4 (25%)	2 (12.5%)	3 (18.2%)	16 (100%)	14 (88%)	2 (12%)

The duration of follow-up in this group varies from 2 months to 12 years.

The over-all picture in this group of cases, then, is excellent immediate and long-term results.

The immediate effect of surgery noted in the cases of blebs complicated by pulmonary emphysema (Table III) was good in all 12 (100 per cent) cases. Six (50 per cent) of these patients noted good late results, while

TABLE III. RESULTS AND DURATION OF FOLLOW-UP IN 12 CASES OF BLEBS COMPLICATED BY EMPHYSEMA

CASE	IMMEDIATE RESULT	LATE RESULT	DURATION OF FOLLOW-UP			OVER-ALL RESULT
			RETURN OF SYMPTOMS	ALIVE WITH SYMPTOMS	DIED	
1. W. M.	Good	Poor	2 mo.	–	9 mo.	Poor
2. A. M.	Good	Poor	6 mo.	–	18 mo.	Poor
3. D. E.	Good	Poor	8 mo.	12 mo.	–	Poor
4. O. R.	Good	Poor	8 mo.	–	24 mo.	Poor
5. T. L.	Good	Poor	10 mo.	36 mo.	–	Poor
6. C. G.	Good	Poor	10 mo.	–	18 mo.	Poor
7. E. A.	Good	Good	3 yr.	7 yr.	–	Poor
8. H. S.	Good	Good	3 yr.	–	4 yr.	Poor
9. R. G.	Good	Good	5 yr.	–	8.5 yr.	Poor
10. W. K.	Good	Good	6 yr.	–	8.5 yr.	Poor
11. J. G.	Good	Good	7 yr.	–	12 yr.	Poor
12. E. M.	Good	Good	8 yr.	–	10 yr.	Poor

6 (50 per cent) noted poor late results. Of those patients classified as showing poor late results, all had a return of their initial symptoms within 2 to 10 months. Two of these are alive with symptoms of progressive emphysema 12 and 36 months after surgery, while 4 died of cor pulmonale 9, 18, and 24 months, postoperatively. The 6 (50 per cent) patients recorded as showing good late results are classified as such only because they did not note a return of their initial symptoms until from 3 to 8 years after treatment. Of these 6 patients, 1 is alive with symptoms of progressive emphysema 7 years later, while 5 died from right heart failure from 4 to 12 years after surgery. The over-all prognosis in this form of the disease is poor in spite of the good immediate result, for all of the patients eventually die of their emphysema.

LOCALIZED VESICULAR AND BULLOUS EMPHYSEMA

Discussion.—In localized vesicular and bullous emphysema, we are confronted with a more complex problem; not only from the standpoint of the altered physiology and the pathology present, but also from the standpoint of the indications for surgery. The rationale of surgery for generalized vesicular and bullous emphysema is different and more complicated than for emphysematous blebs. In this disease the inelastic lungs are simply too large for the thorax. They are crowded into it. This crowding interferes with the mechanics of respiration and circulation. It forces the diaphragm down and out of function. As Brantigan[29, 30, 31] has pointed out, it contributes to the obstruction of the finer air passages and so to a reduced maximum breathing capacity with bronchial infection, cough, and wheezing. The increased pressure on the great veins and auricles produces a relative cardiac tamponade. The lungs are rarely uniformly involved (Fig 7), and those areas most dilated, most inelastic, and most obstructed compress and put out of function the more

elastic and normal lung portions. Operation by resection of the areas most severely involved aims to reduce the size of the lung and so raise the diaphragm, decrease the obstruction of the bronchioles, lessen the pressure on the heart and great veins, and bring the more normal lung portions back into function.

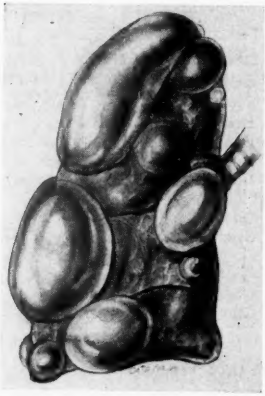


Fig. 7.—In vesicular and bullous emphysema, the lungs are rarely uniformly involved. Those areas most dilated, most inelastic, and most obstructed compress and put out of function the more elastic and normal lung portions. Operation by resection of the areas most severely involved aims to reduce the size of the lung and so to raise the diaphragm, decrease the obstruction of the bronchioles, lessen the pressure on the heart and great veins, and to bring the more normal lung portions back into function.

In his original classical description of emphysema, Laennec[22] pointed out that emphysema rarely involved all lung portions equally—that in nearly all cases some areas were worse than others and that the disease might be limited to one lung, or to one lobe or segment.

In 1951, in a paper read before The Chicago Society of Internal Medicine,[23] we discussed cases of this kind and suggested that there might be relief by surgery. In 1952 we operated upon such a patient and since then have operated upon a total of 19. We have, of course, seen many more cases of emphysema. Most of these patients, however, can be made reasonably functional by medical treatment and/or pneumoperitoneum.

We have selected for operation only those cases in which the roentgenograms revealed that part or parts of the lung were more involved than others. We have not, as Brantigan advises,[29, 30, 31] operated upon patients with generalized disease in order merely to decrease the size of the lungs. While this may be feasible and advisable, we have not dared to do it, feeling that in these cases there was too little normal lung present.

We have chosen to present 3 typical cases to illustrate the indications we have used and the results which can be obtained.

Case Reports

CASE 3.—M. L., CWMH 427042 (Fig. 8). A 55-year-old white female secretary was almost completely incapacitated by dyspnea. She was severely dyspneic at complete rest

and coughed almost constantly. She had grown progressively worse in spite of medical treatment. The roentgenogram revealed emphysema at the bases of both lungs and what appeared to be a large bleb on the right side. She was too dyspneic to undergo pulmonary function studies. At operation on May 17, 1956, the right middle lobe was tremendously dilated by generalized nonbullous emphysema. The apex of the lower lobe was similarly affected. The middle lobe was removed and the apex of the lower lobe was wedged off. Segmental resections are contraindicated in emphysema.

Following operation the cough and wheezing practically disappeared and 6 weeks after discharge from the hospital she was walking 7 miles a day. She returned to work and is working today, 4 years after the operation. In 1958 she underwent surgery for carcinoma of the colon. Although some cough has returned and dyspnea is gradually increasing, she still has a practical respiratory capacity 4 years after surgery.

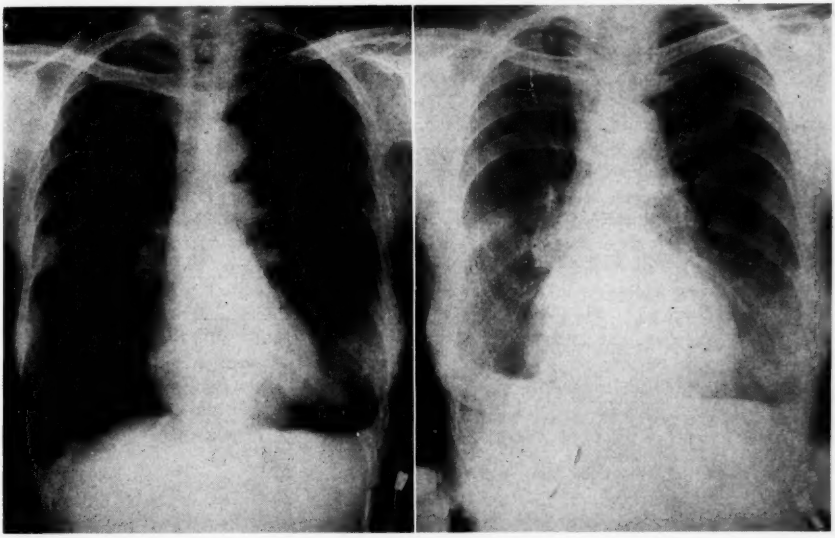


Fig. 8.—Case 3. Pre- and postoperative roentgenogram of a 55-year-old white woman who had a right middle lobectomy and wedge resection of the apex of the lower lobe for localized vesicular (nonbullous) emphysema. Before operation she was almost completely incapacitated. The patient is alive and working 4 years after operation with only minimal symptoms.

Case 4.—H. McK., CWMH 484538 (Fig. 9). This 51-year-old white male high school teacher had noted progressive dyspnea, cough, and wheezing since 1948. The symptoms had progressed to the point that he was barely able to carry on his teaching responsibilities. The roentgenogram revealed what was believed to be contraction and compression of the left upper lobe by a markedly distended and emphysematous left lower lobe. There was also evidence of bullous emphysema in the right lower lobe area. Pulmonary function studies revealed a maximum breathing capacity (MBC) of 29 per cent of predicted normal, a vital capacity (VC) of 58 per cent of predicted normal, a 3-second timed vital capacity (TVC) of 68, 75, and 92 per cent, a residual lung volume (RLV) of 131 per cent of predicted normal, and a R.V./T.L.V. ratio of 50 per cent (30 to 35 per cent normal).

At thoracotomy on Oct. 23, 1958, a large emphysematous portion of lung was seen filling the entire left pleural space. This was found to arise only from the superior segment of the lower lobe. It was removed in wedge fashion along with two smaller areas of similarly involved lung from the lower lobe.

When last seen in April of 1960 the patient was fully engaged in his teaching profession, traveling to educational conventions, and performing his own yard and garden chores with minimal difficulty. Pulmonary function studies on April 27, 1960, revealed a MBC of 47 per cent of predicted normal, a VC of 100 per cent of predicted normal, a 3-second TVC of 40, 50, and 60 per cent, a RLV of 116 per cent of predicted normal, and a R.V./T.L.V. ratio of 34 per cent (30 to 35 per cent normal). We have never seen a patient more pleased with the results of surgery. It has been our experience that frequently the objective function studies do not reveal the excellent subjective clinical improvement noted by the patients.

CASE 5.—F. H., CWMH 484503 (Fig. 10). This 51-year-old white housewife had been bothered by cough, sputum production, dyspnea, and wheezing for 10 to 12 years. For the past 2 to 3 years she had noted progressive dyspnea which had become especially severe after an attack of pneumonia 2 to 3 months before admission to the hospital. She was incapacitated to the point where she was unable to do any housework. She had been cyanotic for many years. A roentgenogram revealed generalized emphysema with a very large bleb-like appearing area occupying the entire lower one half of the right pleural cavity. Bronchogram revealed universal bronchiectasis. She was unable to tolerate pulmonary function studies.

On Nov. 19, 1958, a tracheostomy was performed and the patient placed on a mechanical respirator (Mörch). At the time of tracheostomy the patient's blood was almost black in color. With the institution of mechanical respiration the cyanosis disappeared and she was much more comfortable. On Nov. 25, 1958, with respiration being maintained by the mechanical respirator, operation was performed and a tremendously enlarged, emphysematous right middle lobe was found to be compressing the remaining lung portions. The middle lobe was removed and the patient was maintained on the mechanical respirator for several weeks postoperatively. When she resumed her own respiratory activity, she found her breathing much easier and upon returning home she was eventually able to resume her household duties. She remains much improved with regard to her dyspnea, but continues to be bothered by cough and sputum production, secondary to her universal bronchiectasis. When last seen in February of 1960 she was in early right heart failure. This has been controlled temporarily and her cough and sputum production have improved on medical management. Although temporarily much improved by surgery, the eventual outcome of this case is obvious.

Operative Mortality and Type of Surgery.—In the group of 19 cases (Table IV) there were 4 (21 per cent) operative deaths: 1 from right heart failure, 1 from thrombosis of the pulmonary vein, 1 from a Pseudomonas pneumonia, and 1 patient died suddenly 6 days after discharge from the hospital.

TABLE IV. OPERATIVE MORTALITY AND TYPE OF SURGERY IN 19 PATIENTS OPERATED UPON FOR LOCALIZED VESICULAR OR BULLOUS EMPHYSEMA

NO. OF CASES	OPERATIVE MORTALITY	TYPE OF SURGERY		
		MONALDI	MONALDI + RESECTION	RESECTION
19	4 (21%)	1 (5.3%)	2 (10.5%)	16 (84.2%)

One (5.3 per cent) of the patients had been treated by Monaldi's suction alone, 2 (10.5 per cent) were treated by Monaldi suction plus resection, and 16 (84.2 per cent) were treated by pulmonary resection alone.

Results and Follow-up Evaluation.—Inasmuch as the cases vary so greatly both in regard to indications and the degree and length of improvement, it has proved impossible to classify them and present them in the form of a concise chart (Table V). Three cases have already been reported in detail.

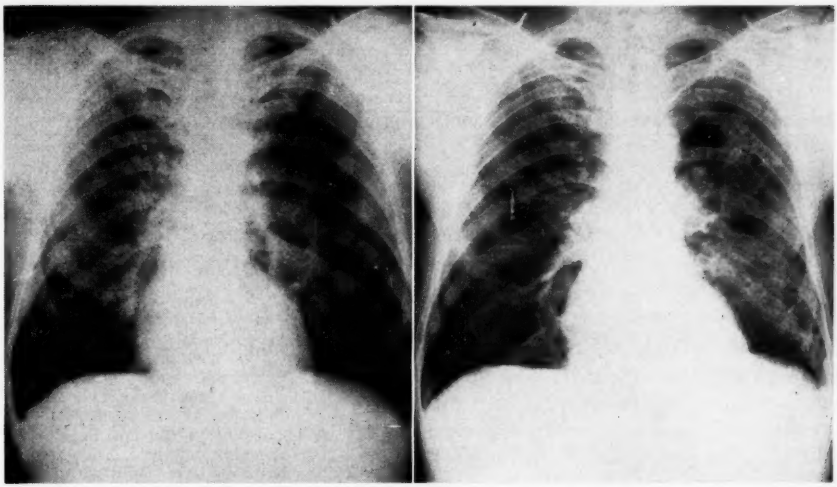


Fig. 9.—Case 4. Pre- and postoperative x-ray studies of a 51-year-old white male high school teacher. At thoracotomy a large emphysematous portion of the lung was found to be filling almost the entire left pleural space. This emphysematous lung arose only from the superior segment of the lower lobe and was compressing the remaining lung tissue. It was removed in wedge fashion.

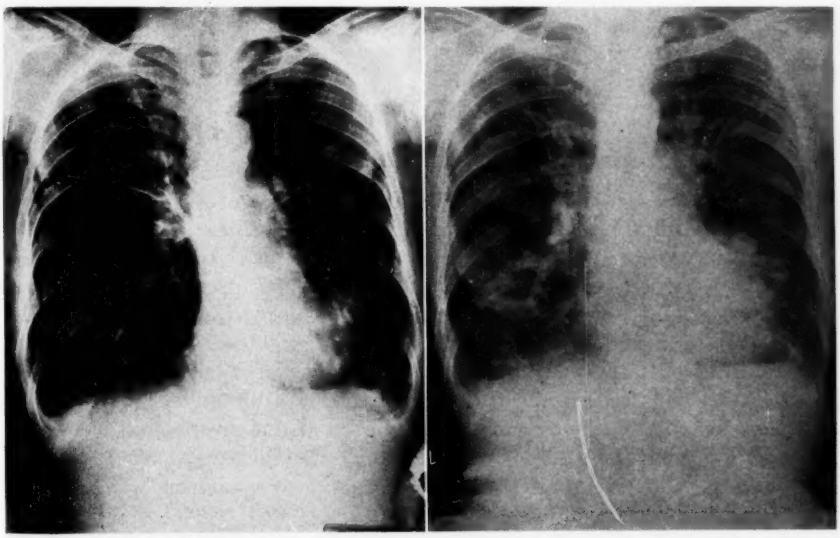


Fig. 10.—Case 5. Pre- and postoperative x-ray studies of a 51-year-old white woman. Symptoms had been those of progressive dyspnea, cough, and sputum production for 10 to 12 years; more severe since an episode of pneumonia 2 to 3 months prior to admission. The films show emphysema and a bleb-like area in the lower two-thirds of the right lung field. Bronchograms revealed universal bronchiectasis. At thoracotomy, with the patient maintained on a mechanical respirator, a markedly emphysematous middle lobe was resected. Thereafter, she was markedly improved, but has shown signs of early cor pulmonale 18 months after the operation.

TABLE V. RESULTS IN 19 PATIENTS OPERATED UPON FOR LOCALIZED VESICULAR OR BULLOUS EMPHYSEMA

CASE NO.	AGE	RACE	SEX	DATE OF SURGERY	POSTOP. DEATH	IMMEDIATE RESULTS			LATE RESULT: DATE SYMPTOMS RETURNED, DATE OF DEATH, AND PRESENT STATUS
						E	G	P	
367716	62	W	M	9/12/53	3			X	Operative death, Pseudomonas pneumonia
466035	65	W	M	1/11/58	26			X	Operative death, sudden death at home
474563	36	W	M	5/10/58	22			X	Operative death, pulmonary thrombosis
500669	57	W	F	7/9/59	3			X	Operative death, right heart failure
309197	22	W	M	3/15/50		X			Asymptomatic April, 1960; 10 yr. postop.
484538	51	W	M	10/23/58		X			Asymptomatic April, 1960; 8 yr. postop.
468852	68	W	M	2/16/58			X		Symptom return 3 mo. postop.; died 4 mo. postop.
423273	52	W	M	10/4/57		X			Symptom return 3 yr. postop.; died 3 yr. postop.
516345	56	W	M	2/22/60			X		Remains improved 3 mo. postop.
510871	58	W	M	2/8/60			X		Remains improved 3 mo. postop.
507580	64	N	F	11/6/59			X		Remains improved 6 mo. postop.
11789	56	W	M	4/9/59			X		Symptom return 4 mo. postop.; now progressive
511734	58	W	M	2/23/59		X			Symptom return 6 mo. postop.; now progressive
412890	46	W	M	7/27/55			X		Symptom return 7 mo. postop.; now progressive
508893	49	W	M	5/18/59			X		Still some dyspnea 1 yr. postop.
484503	51	W	F	11/25/58		X			Cor pulmonale 1 yr. postop.
442967	45	W	F	4/21/54			X		Symptom return 2 yr. postop.; now progressive
508608	54	W	M	9/10/52		X			Symptom return 3 yr. postop.; now progressive
427042	55	W	F	5/17/56		X			Still working 4 yr. postop.; mild symptoms

One of these patients whose emphysema was limited to one segment and another one with a tremendously emphysematous accessory lobe appear to be permanently cured. Two patients have died of progressive disease 5 months and 3 years, respectively, since operation. Three patients have been followed for a maximum of 6 months, and remain much improved at the present time. The remaining 8 patients have had a return of symptoms from 4 months to 4 years after operation. Of these, only 1 does not show signs of progressive deterioration and she is actively employed 4 years after pulmonary resection.

Here again, as in the patients operated upon for emphysematous blebs complicated by generalized emphysema, although the immediate result may be excellent, the patients usually have a return of their symptoms which become progressive and eventually cause their death.

SUMMARY AND CONCLUSIONS

Fifty cases of emphysematous blebs and localized vesicular and bullous emphysema treated by Monaldi intracavitary suction or open surgical resection are reported.

The cases are divided into two groups. The first includes cases of emphysematous blebs complicated or uncomplicated by generalized emphysema. The second includes all cases of localized vesicular and bullous emphysema. At the present time, although it may be advisable, we have not operated upon patients with generalized disease alone, feeling that in such cases there is too little normal lung present.

The surgical indications for each group are defined and illustrative cases are presented. The open operation has become the preferred surgical approach in most instances. The operative mortality for the entire group was 8 per cent.

The immediate and late results are tabulated. In those cases of emphysematous blebs uncomplicated by generalized emphysema, the immediate effect is excellent and permanent. In spite of an excellent early result, patients with blebs complicated by generalized emphysema and those with localized vesicular and bullous emphysema note a return of their symptoms at varying periods of time. These symptoms then become progressive and the majority of cases terminate in right heart failure. However, these discouraging results in such patients should not deter us from operating upon them, for they are markedly benefited over a significant period of time by resection of the most severely involved areas.

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DISCUSSION

DR. JOSEPH GORDON, Albuquerque, N. Mex.—I should like to tell you about our very limited experience in a small group of cases in New Mexico at the Veterans Administration Hospital.

This problem has been very well presented in the previous paper, and it is a difficult one in which we are still trying to find our way. The group of patients which we have studied were operated upon by Dr. Wesley Childs, who was then Chief of Service and is now associated with Dr. Charles Bailey.

The patients were all severely distressed. They had a maximum breathing capacity of under 30 per cent, and these were patients who were unable to get around. Since they were veterans they were hospitalized and remained almost incapacitated in their present condition.

This problem does not lead us to find our way directly, because of the admixture of such things as diffuse emphysema, solitary cyst, and bullae that may occur in one individual. I have chosen the slides of one particular case to show you what our experience has been in this instance, from which some help has been drawn.

(Slide) The x-ray film which you see is not unlike some of those which were shown previously. On the right side there is a giant-sized space-occupying emphysematous bulla or bleb, as we may choose to term it. This is a matter of definition. On the other side in the left lower third of the chest, there are multiple cystlike changes in contrast to the right side.

Following this, bronchograms were done which you will see in the next slide. (Slide) On the right you see the evidence of the space-occupying bullous emphysema with constriction of the bronchial tree. On the left side there is evidence of a relative paucity of bronchial arborization.

The patient was operated upon on both sides. On the right side, an upper lobectomy was done. Prior to this the patient had a maximum saturation of 84 per cent oxygen in his blood; after this he had a 92 per cent oxygen saturation. On exercise the unusual observation was made that it became 94 per cent, indicating that there had been improvement in circulation.

Some time later the left lung was operated upon by oversewing of the emphysematous blebs rather than by excision. However, after this second operation the patient showed some deterioration, and I should like to show you in the next slide what we have noted in the bronchogram.

(Slide) There is good reorientation of the bronchogram on the side on which operation was followed by good results, and there is poor reorientation on the left side, on which operation was followed by further deterioration in the patient. It is to be concluded that the reorientation of the bronchial tree to a more nearly normal pattern was followed by marked functional improvement. The poorer bronchogram seen on the second or the left side following operation was accompanied by deterioration in functional capacity.

DR. W. EMORY BURNETT, Philadelphia, Pa.—It is a great opportunity on this occasion to hear about these remarkable experiences with this miserable and progressive disease.

Since the senior author suggested two-stage drainage several years ago, we have all used it now and then because it has a very useful purpose. It permits improvement with very little surgery in some of these poor risk patients and permits of multiple attack which is also a great advantage. It has been a very helpful method.

(Slide) The combinations mentioned today have been extremely useful in our hands as well as theirs; (slide) namely, on this upper lobe situation. They have prolonged patients' lives indefinitely, although ordinarily it is a progressive disease with a miserable outcome.

In some, as you see here (slide), there is a fairly localized disease with a large bulla on one side and a fairly good lung on the other. It certainly seems wise to operate and remove the diseased area. Some of these patients have received tremendous benefit.

(Slide) This same patient, 5 years later, shows some further progression but has had a greatly improved function in the interim and even at this time.

When the disease is bilateral, but more marked on one side than the other, one also finds it worth while to operate. Occasionally, one is surprised to find that the disease is almost completely confined to one lobe which can be removed. In these situations one can produce excellent temporary benefit.

(Slide) Finally, I'd like to call attention to the fact that a marked degree of obstructive emphysema may accompany carcinoma which may be overlooked. Such a condition is readily demonstrated by inspiration-expiration films and one should be on the watch for such a lesion.

(Slide) Last, I'd like to call attention to the fact that a marked degree of destructive emphysema may accompany carcinoma which may be overlooked.

DR. OTTO C. BRANTIGAN, Baltimore, Md.—I would like to call attention to two points: First, there is a disturbance in vascularity. The slide shows an emphysematous lung with the pulmonary artery injected. It shows the disturbance to be primarily in the capillaries of the alveoli. Second, in primary hypertrophic obstructive bilateral pulmonary emphysema, there is obstruction to the outflow of air from the lung. There is no known etiology and there is controversy about the initial cause of airway obstruction, but in the later stages of the disease there is obviously an interruption of the physiologic mechanism that holds open the bronchioles. The physiologic principle involved in holding open the collapsible bronchioles depends upon an elastic lung which is held expanded by a rigid chest wall and a closed pleural space. The elasticity of the lung causes a negative intrapleural pressure and a circumferential force that holds open the bronchioles. Normally, on inspiration, bronchi and bronchioles enlarge in diameter; on expiration, they decrease in diameter. When primary emphysema, with or without blebs, or bullae, is fully developed, the loss of this physiologic principle is an important factor in expiratory airway obstruction, regardless of its etiology or initial cause. In primary hypertrophic obstructive bilateral pulmonary emphysema, with or without blebs, or bullae, the expiratory volume of the lung is much larger than normal. Pulmonary emphysema is similar to stuffing 6,000 or 7,000 c.c. of lung into a pleural space of 5,000 c.c. volume. In such a situation, the circumferential pull holding open the bronchioles is lost to a greater or lesser degree.

It would seem that in any surgical attack upon the disease, one must return this lost physiologic mechanism and it can be done in some degree by reducing the lung volume.

Dr. Head indicated that their patients, by the progression of disease after operation, lost the benefit gained by surgery. I would like to call attention to the fact that pulmonary emphysema is a bilateral disease. If both sides are not operated upon, there will be progression of disease in the unoperated lung. I suspect their patients will show progression of disease in the unoperated lung when the benefit gained by the first operation is lost. In the patients whom I have operated upon, there has been no progression of disease in the lung operated upon. At the present time there has been no loss of benefit gained by operation in the patients that have had bilateral operations. The longest follow-up is 8 years. In time, there must be some loss of benefit gained by surgery since emphysema is a disease of aging.

DR. OSLER ABBOTT, Atlanta, Ga.—Our group has had a major interest in this problem for some 15 years. We cannot concur in "the horrible long-term outlook" expressed by Dr. Head and his co-workers. Certain patients have had purely isolated bullous disease associated with normal lung. In this group, adequate excision has not been followed by the appearance of any progressive pulmonary degenerative process. In the other group in which bullous emphysema and the so-called hypertrophic obstructive type of emphysema is combined, we have not seen "progressive deterioration." Fundamentally, the problem is that surgical excision of bullae compressing adjacent areas of hypertrophic obstructive emphysema is only a part of the total treatment of this latter disease. In many instances, appropriate concomitant pulmonary denervation should be done. In all instances, a continuous, assiduous, and vigorous over-all nonsurgical treatment regimen must be instituted and continually monitored. Such a regimen must include (a) total abstinence from tobacco, (b) separation from other known sources of bronchial irritation, (c) control of associated bronchial infection and allergies, (d) refunctionalizing intercostal and diaphragmatic exercises, (e) bronchodilators, (f) expectorants, and (g) other supportive measures as indicated. To expect surgical procedures alone to stem the progress of pulmonary emphysema would appear to be a misunderstanding of one of the basic principles in the management of any type of chronic disease due to a combination of multiple causative factors.

At the present time, we have embarked on a prolonged study of emphysema therapy. We start with an extensive objective evaluation program including (a) roentgenograms, cinefluoroscopy, and pulmonary angiography, (b) cardiac catheterization, and (c) complete pulmonary function tests. At yearly intervals these tests are repeated. Four protocols of treatment used include: (1) steroids, chemotherapy, chest exercises, and bronchodilators, (2) the same combination as No. 1 plus multiple bronchoscopy, (3) multiple bronchoscopy, expectorants, chest exercises, bronchodilators—but no steroids, and (4) the same regimen as No. 3 plus surgical excision of localized advanced areas of disease plus pulmonary plexectomy.

The principle on which we base surgical therapy is that "when the finer pulmonary vasculature persists in patients with hypertrophic obstructive emphysema, there also is found persistence of the other components of the lung essential for useful respiratory function." A corollary to this principle is that "pulmonary emphysema is initially a disease of single or multiple major foci and the reflection of this primary localization persists even in terminal cases."

In view of this attitude we now place an increasingly major interest in pulmonary angiography. If such studies show compression of areas of the lung containing finer vascular components, then removal of an avascular area of lung distended by diffuse obstructive emphysema will release a potentially useful area. At surgery the effect of blockade of the pulmonary autonomic nervous system is studied. We study initially the effect of such blockade upon the per stroke volume of air delivered by "pressure constant, volume variable" ventilation assistor. Second, we are interested in the effect upon the gradient between the pulmonary artery and the venous pressure. Third, we study the effect upon the mean pulse pressure of the pulmonary artery and venous tracings. If sufficient beneficial functional

response is noted in these studies, we add a pulmonary plexectomy to the selective excision of distended nonfunctioning lung tissue. In our experience, the postoperative course of these patients is often difficult, but controllable. Mortality rate is within reasonable limits. Long-term benefits have been obtainable, but attention to continued intensive prophylactic, rehabilitative, and therapeutic measures is mandatory.

DR. RICHARD H. OVERHOLT, Boston, Mass.—Dr. Head and his associates have clearly pointed out the manner by which structural defects alter the movement of air, its occupancy within, and availability of diffusing surfaces. The value of pre- and postoperative respiratory assistance has been stressed, if borderline cases are to be accepted for surgery.

Now, regardless of the extent of the structural changes, many patients have their functional capacities further reduced by an irritated air tube system. Mucosal swelling causes narrowing, and excessive secretions occlude or spill over to cause spasms of other bronchi. Countless check valve mechanisms then operate at the bronchiolar level. These are the net effects of a chemical bronchitis induced by the inhalation of tobacco smoke.

They are reversible. A period of 2 to 6 weeks usually results in substantial improvement. Many cases which we previously rejected on grounds of functional inadequacy now are being accepted. Even in good risk patients the convalescence is smoother if there is a period of freedom from chemical irritation in advance of the intervention. Many of the patients with poor pulmonary function learn this and have already stopped smoking before we see them.

Now, Dr. Head's experience and that of others' with generalized emphysema bear out that it is very difficult to correct it by surgical means. Fortunately, this disabling pulmonary disease can be prevented. Dr. Lowell and others have called attention to the fact that simple diffuse emphysema is usually an acquired disease. In the great majority of cases it represents a lung worn out by years and years of filtering out tobacco tars. Surgeons can relieve more suffering and prolong the lives of more people by advice on the prevention of emphysema than they can by the skillful application of the scalpel.

DR. WILLIAM M. TUTTLE, Detroit, Mich.—I just want to say one thing which I think has been missed in much of this discussion, and that is that emphysema is, after all, a result of aging, and aging can come differently to different people. Some people age much younger than other individuals. As you lose the elasticity of your alveoli, you also are probably losing it in your face. You become more wrinkled and you become more tired-looking, like I do. [Laughter]

However, I do agree with the authors that the removal of individual large blebs or emphysematous cysts, whichever you want to call them, is a fortunate thing, and I think it works. I think to operate bilaterally on emphysematous individuals is a perfectly foolhardy situation, and I do not think any surgeon should do it. I feel that you must consider emphysema, and realize that some of these individuals must be told that they will have to live with their emphysema, which they are going to have to do. Furthermore, there is no question in my mind that until tobacco has been proved to be a cause we should leave the matter out.

Now, I was once on a program with Dr. Overholt in which he criticized me for smoking, and I told him that my mother had once told me, "If you are not afraid of anything, you will never catch it," and I never did. [Laughter and applause]

PRESIDENT ADAMS: Many of you don't appreciate that the discussions at the present time are far different than what they were 20 years ago. Dr. Tuttle is injecting into this discussion something of the controversy and the argument that we used to see very often.

DR. HUDSON (Closing).—I think there probably will be no exception taken to the statement that blebs, bullae, that occupy much space or that cause much shortness of breath or that can be shown to be increasing with serial x-rays, should be resected. When these situations are complemented by what I like to call chronic obstructive pulmonary emphysema, the situation becomes entirely different, and this is where the argument begins.

It is my feeling that people with chronic obstructive pulmonary emphysema should be operated on only after a thorough, thoughtful consideration of each case, both from a physiologic standpoint and also from a socioeconomic standpoint. This is very important not only to the individual but to his family group.

As surgeons, we rarely see chronic obstructive pulmonary emphysema except when it's got to its final or surgical point. I agree with Dr. Overholt and Dr. Abbott, and the others that have mentioned it, that there is a point in chronic obstructive pulmonary emphysema where it is reversible. I don't know just where this point is, but I base this experience on several patients who have studies indicating severe pulmonary emphysema without discernible changes in the lungs on the roentgenogram.

By taking these patients off cigarettes and by giving them the various things that the medical men give them for this disease, they have become rehabilitated and have continued to lead good lives without shortness of breath.

I would like to thank all the discussers for their interest, and I believe we too have learned something from them.

LUNG ABSCESS IN JAPAN

Kingo Shinoi, M.D. (by invitation), Tokyo, Japan*

SINCE 1935, I have had the opportunity to observe nearly 2,000 patients under treatment for various types of lung disease: composed of 1,200 cases of tuberculosis, 551 cases of lung abscess, 210 cases of lung cancer, 105 cases of bronchiectasis, and 30 cases of miscellaneous conditions. In these patients I have made special studies of lung abscess, which I wish to present on this occasion.

I. ETIOLOGY OF LUNG ABSCESS SEEN IN JAPAN

Analysis of 19,916 autopsy records, collected from the principal medical colleges in Japan, reveals that lung abscess was present in 638 cases. The putrid type of lung abscess was seen in 44 per cent of these—the non-putrid type in 56 per cent. However, the data in my clinic indicate that the putrid type has been found in 95 per cent of all cases, since the majority of patients suffering from the non-putrid type of the disease, which is hematogenous in origin, either die with their disease undiagnosed or recover by chemotherapy (Table I).

TABLE I. LUNG ABSCESS IN JAPAN

	AUTOPSY CASES	CLINICAL CASES
Putrid	282 (44%)	523 (95%)
Non-putrid	356 (56%)	28 (5%)

In 1938, I demonstrated experimentally that this disease was produced mainly by bronchoembolism, but 53 per cent of the patients treated in my clinic had developed the disease by aspiration of undetermined nature as shown in the Table II, and 76 per cent of these showed evidence of dental disease. The postoperative incidence was only 5.1 per cent, much lower than in Europe and America. This may be attributed to the relatively infrequent use of general anesthesia, which is practically never used in oral surgery.

II. PATHOLOGIC STUDIES

Lung abscess, especially in the chronic stage, is essentially a state of pyofibrosis in which abnormal proliferation of bronchial mucous epithelium occurs.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

*Professor of Surgery, Tokyo Medical College, Tokyo, Japan.

TABLE II. ETIOLOGY OF LUNG ABSCESS IN JAPAN

Aspiration of unknown cause	53.0%
Foreign body	5.1%
Postoperative	5.1%
Vomiting due to gastrointestinal and brain diseases	5.1%
Diseases of oral cavity, nose, and pharynx	2.1%
Bronchiectasis	12.4%
Tuberculosis	5.5%
Bronchial tumor	15.0%
Injury	0.4%
Perforation of esophageal carcinoma	0.4%

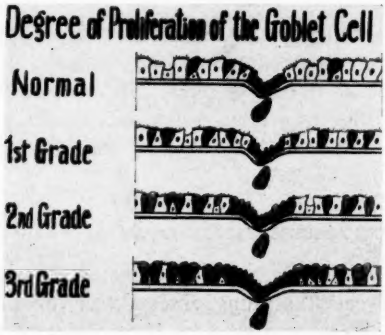

Fig. 1.—Degree of proliferation of the goblet cell. (Goblet cell is indicated as black cell.)

Such proliferative processes may involve columnar proliferation, squamous metaplasia, atypical proliferation, adenomatous metaplasia, and hyperplasia of goblet cells, all of which, excepting the proliferation of goblet cells, must be regarded as constituting carcinogenic matrices. Proliferation of columnar epithelium is chiefly encountered in large and medium bronchi, as shown in Table III, squamous cell metaplasia and atypical proliferation in the cavity wall, and adenomatous metaplasia in the bronchioles.

TABLE III. PROLIFERATION OF EPITHELIUM AND ITS SITE OF ORIGIN IN BRONCHUS

	LARGE	MEDIUM	CAPILLARY	CAVITY WALL
Columnar	84.3%	88.5%	3.8%	13.5%
Squamous	2.3%	23.1%	0	83.8%
Atypical	0	0	0	0
Adenomatous	0	0	53.8%	0
Cancerous			1.3%	

Careful search was made for carcinoma in situ and only one instance of minute carcinoma was found in 71 cases. This was detected in the region presenting adenomatous metaplasia of a chronic inflammatory lesion, accompanied by bronchiectasis in the left lower lobe, and was only as large as a millet grain. Although the incidence is only 1 per cent, there is a possibility of such a focus furnishing a carcinogenic matrix.

The significance of goblet cell proliferation in the production of sputum requires comment. These cells are normally present in relatively large numbers around the orifices of the mucous gland but, in this location, they are

found in the proportion of one to ten of ciliated epithelial cells, as shown in Fig. 1. In pyofibrous lesions, however, the goblet cells are greatly proliferated, the degree of hyperplasia being designated as first grade in which the proliferative ratio of ciliated epithelium to goblet cells is 5:1, the second grade with the ratio of 3:1, in which the goblet cells show swelling, and the third grade with predominance of the mucus-filled goblet cells, some even suggesting the mucous membrane of gastrointestinal tract, as illustrated in Fig. 1. In lung abscess and bronchiectasis the proliferative changes are mostly of the second and third grades, being much more marked in other diseases, as shown in Table IV.

TABLE IV. DEGREE OF PROLIFERATION OF THE GOBLET CELL IN VARIOUS LUNG DISEASES

	ABSCESS	BRONCHIECTASIS	TUBERCULOSIS	CANCER
Normal	15.4%	10.0%	63.3%	66.7%
1st Grade	40.5%	20.0%	26.7%	33.3%
2nd Grade	30.8%	30.5%	10.0%	0
3rd Grade	13.4%	35.0%	0	0

As to relation of the proliferation of goblet cells to sputum production, it is evident that quantities of sputum exceeding 100 c.c. are associated with the second and third grade proliferation, whereas those of 50 c.c. or less are associated with either the first grade or normal, as shown in Table V. The

TABLE V. RELATION BETWEEN SPUTUM VOLUME AND PROLIFERATION OF THE GOBLET CELL

	0-10 c.c.	10 c.c.-50 c.c.	50 c.c.-100 c.c.	100 c.c.-200 c.c.
Normal	40.0%	5.8%	0	12.5%
1st Grade	46.6%	52.9%	16.6%	23.0%
2nd Grade	13.4%	35.2%	50.0%	35.0%
3rd Grade	0	5.8%	33.0%	27.0%

sputum expectorated during the chronic stage contains more mucus with a higher pH but lower viscosity and specific gravity because of a lower protein content, when compared with that of the acute stage. These findings indicate that the goblet cells are intimately concerned with the production of sputum rich in mucus during the chronic stage.

III. SOME CLINICAL PROBLEMS

Of 551 cases of lung abscess treated in our clinic, 338 patients belonged to the preantibiotic age and the remainder to the postantibiotic age; the two groups show definite differences in many ways. The incidence of silent abscess or recurrent abscess is high in the former group, presenting variable clinical pictures. On the other hand, complications, such as cerebral abscess or empyema, are apparently decreased. Bacteria found in the sputum are usually fuso-spirochetal in type during the acute stage, often changing to drug-resistant staphylococcal type, probably the result of long-continued ineffective chemotherapy.

Operative intervention is indicated in patients with chronic disease who have had chemotherapy up to 1 month. It is important to bear in mind in proceeding with the operation that the chronic cases are wet cases complicated by lowered cardiopulmonary function.

Thus, in chronic recurrent cases of lung abscess, the alveolar function is reduced when fibrosis of the lesion occurs extensively, and, in cases characterized by abundant sputum, the disturbance of ventilation leads to latent anoxia and produces an additional load on the right heart.

In determining the indication for lung resection, the functional limits should be set at 40 per cent or over of vital capacity, 61 per cent or less of residual air, 82 per cent or more of ventilatory reserve ratio, 85 per cent or over of arterial oxygen saturation, and 20 mm. Hg or less of pulmonary arterial pressure, as shown in Table VI. These requirements are therefore far more strict than in lung resection for tuberculosis.

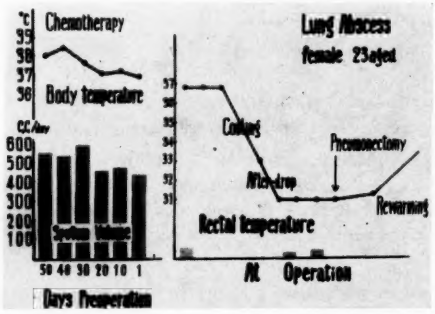

Fig. 2.—Quantities of bronchial secretion before and after operation under hypothermia.

TABLE VI. INDICATION FOR OPERATION OF WET CASE

Per cent of predicted vital capacity	more than 40 %
Residual volume/total lung capacity 100	less than 60%
Ventilatory reserve ratio	more than 82%
Sao_2	more than 85%
Pulmonary arterial pressure	less than 20 mm. Hg

The pulmonary capacity is reduced upon cessation of sputum production after lung resection, but both ventilatory and alveolar function are markedly improved, although no immediate amelioration of the circulatory burden occurs.

Disposal of secretion discharged during the operation on a wet case, such as a lung abscess, is an important problem for consideration. It is desirable to convert the disease into a dry case preoperatively by means of chemotherapy, bronchial lavage, and postural drainage, but if these measures are ineffective the application of artificial hypothermia is utilized. With the reduction of rectal temperature to 30° C. or lower by cooling the entire body, the secretion of the air passage ceases and operation can be performed in a dry state. Fig. 2 is a chart of a patient with a lung abscess of the entire right lung, who

expectorated as much as 500 c.c. of sputum daily, in whom the respiratory tract becomes so free from secretion under general hypothermia that operation could be performed without difficulty.

Animal experiments show that bronchial secretion is decreased by reason that gastric secretion declines under hypothermia (Fig. 3). Bronchial ciliary movements are depressed (Fig. 4). Moreover, extracellular fluid of the lung is less in the state of hypothermia (Fig. 5).

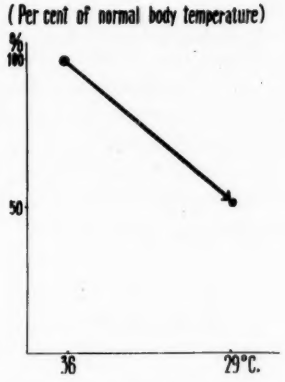

Fig. 3.

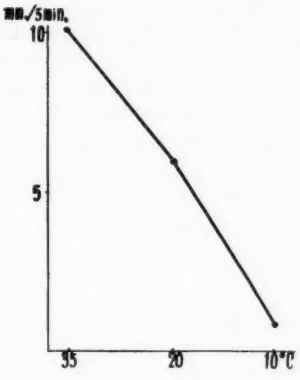

Fig. 4.

Fig. 3.—Influence on gastric secretion in hypothermia.
Fig. 4.—Bronchial ciliary movement (mm. per 5 min.) in hypothermia.

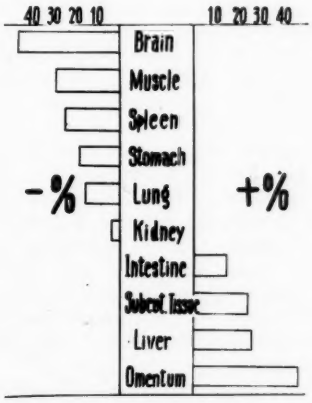

Fig. 5.—Change of extracellular fluid in hypothermia.

Table VII summarizes the therapeutic results which indicate that, before the advent of antibiotics, 13 per cent of patients responded to chemotherapy, 35 per cent to intratracheal administration of iodized oil, and 54 per cent were cured by pneumonotomy, with a mortality rate of 40 per cent.

TABLE VII. RESULTS OF TREATMENT

METHOD OF TREATMENT		CURE RATE	MORTALITY RATE
Preantibiotic			
Chemotherapy	86	13%	34%
Iodized oil	155	35%	
Pneumonotomy	131	54%	40%
Postantibiotic			
Chemotherapy	81	65%	4%
Pneumonotomy	27	60%	20%
Lung resection	100	96%	4%

However, 65 per cent of patients treated with antibiotics showed satisfactory improvement, and pneumonotomy produced cure in 60 per cent. Most of the patients were subjected to lung resection with a cure rate of 96 per cent.

The incidence of postoperative empyema is 23 per cent, a complication commonly encountered in cases of drug-resistant lung abscess. It may be stated in conclusion that most of the patients operated upon in Japan belong to the drug-resistant group, but it is now possible to achieve complete cure of this disease by proper change from chemotherapy to surgery.

DISCUSSION

DR. W. EMORY BURNETT, Philadelphia, Pa.—I want particularly to thank Dr. Shinoi for coming such a great distance to give us the benefit of his extensive experience with this dangerous disease.

In our own experience this had been for several years an almost unknown lesion at Temple University Hospital, until the last 3 or 4 years, during which time there has occurred a progressive increase in admissions for lung abscess. This may be due to the increase in resistant staphylococci, either alone or in combinations—more resistant than they were in the earlier group of lung abscesses, of which there were 115.

From my report some 20 years ago in the *Pennsylvania Medical Journal,* I wish to recall an extremely useful adjunct to treatment; namely, aspiration under fluoroscopy with instillation of high concentrations of antibiotics directly into the cavity. Such concentrations can never be reached by systemic administration and the insulation from the blood stream of this dead tissue makes the contrast even greater.

(Slide) This patient was admitted 10 days after he had been chilled in a cold rain while changing an auto tire, and one sees an obvious abscess which progressed to this marked degree in the period of the next 3 weeks (slide) on systemic antibiotics.

(Slide) The next slide presents the picture 5 days later. Starting on the date of the previous roentgenogram, the patient had two aspirations on consecutive days with the removal of some 50 c.c. of odorous pus the first time and the second time obtaining air only without pus. In each instance 500,000 units of penicillin was injected plus one gram of streptomycin on the second occasion. The temperature dropped to normal in 2 days, and expectoration was reduced almost completely. One can see the rapid improvement in these few days by roentgenograms also.

(Slide) Five months later he appears to be well clinically and by x-ray studies.

(Slide) We also noted that bronchograms of these patients, who were treated in this fashion early in their course, showed no residual bronchiectasis as seen in this instance. (Slide) On this slide of 9 patients successfully treated in this fashion, I would like you to notice how few aspirations were required for each patient—only two or three in most instances.

(Slide) There were 4 others in this series in which there was inadequate diagnosis, pneumothorax, or, in one instance, a slow response in which open-surgery had to be done.

Of the potential complications, pneumothorax occurred in 2 patients. One had apparently received adequate effect of previous aspirations and rapidly recovered. The other had not and required surgery, as listed in the 4 requiring surgery.

Hemoptysis did not occur, possibly because of the accuracy of guidance into the cavity by fluoroscopy. It should be insignificant if it did occur.

Empyema, although feared greatly in the early cases, was not encountered. Possibly this was because of the injection of antibiotic solution throughout the entire withdrawal of the needle to spill the last few drops on the skin, thus decontaminating at the same time that contamination occurred. Neither was air embolism observed. For details I would refer you to the article "Pulmonary Suppuration" (Pennsylvania M. J. 40: 1045-1051, 1937).

(Slide) Chronic abscess, of course, has to be resected without question, but one can clean it up considerably by the same method and produce a state of better nutrition for the patient and less chance of postoperative infection.

If you are unfortunate enough to see an occasional abscess again, I should like to highly commend to you this simple and promptly effective method.

PROFESSOR SHINOI (Closing).—Thank you very much for the discussion.

However, I cannot answer in detail because my English is poor, but I wish to make additional studies of this problem.

A STUDY OF ESSENTIAL HEMOPTYSIS

Raymond J. Barrett, M.D., and William M. Tuttle, M.D., Detroit, Mich.

HEMOPTYSIS is correctly considered to be an ominous sign by physician and patient alike. In from 82 to 96 per cent of various reported series it has been found to be associated with serious underlying disease (Table I). The exact incidence of each lesion cannot be accurately determined since the structure of most reported series is somewhat specialized. However, carcinoma, bronchiectasis, and tuberculosis are the three most common underlying disease processes. Broncholithiasis, bronchial adenoma, foreign bodies, pneumonia, lung abscess, pulmonary infarction, and cardiovascular disease account for most of the remaining cases. Hemoptysis of undetermined origin, the subject of this discussion, varies from 3.8 to 18 per cent in reported series.

TABLE I. INCIDENCE AND ETIOLOGY OF HEMOPTYSIS

LESIONS	PER CENT OF INCIDENCE					
	HELLER (416)*	SOUDERS (105)	MOERSCH (200)	ABBOTT (497)	JACKSON (436)	LEVITT (683)
Bronchial carcinoma	2.4	2.8	29.5	21	20	12
Chronic bronchitis	15	14	9	2	17	—
Bronchiectasis	7	28.5	26.5	21	32	15
Tuberculosis	40	1.9	5.5	22	—	50
Pneumonitis	6	—	3	1	6	1
Lung abscess	1	—	5	—	11	6
Cardiovascular	2	4.7	—	1.4	—	7
Other	1.5	31.1	14	27.8	6	4
Unknown	15	18	7.5	3.8	8	5

*Number of cases.

With such a serious potential, hemoptysis warrants an adequate diagnostic work-up regardless of its extent and whether it has ceased. A negative roentgenogram of the chest in no way relieves the physician of the responsibility for a determined effort to determine the cause of the bleeding. Bronchoscopy and, if negative, bronchography, along with study of the aspirate for tubercle bacilli and malignant cells, constitute a minimum study. Equivocal hilar shadows may require fluoroscopy, laminography, and angiocardiography to settle the question of hilar vessel prominence versus disease process. If the vascular dynamics within the pulmonary tree are suspect as the cause of bleeding, cardiac catheterization may be indicated. There will arise certain instances wherein the

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physician is not convinced that the blood is actually originating from the tracheobronchial tree. In such circumstances, barium swallow, esophagoscopy, and study of the oro- and nasopharynx and sinuses would be in order.

When one has exhausted the diagnostic armamentarium to no avail, the case is variously labelled as idiopathic hemoptysis or hemoptysis of undetermined origin. Speculation as to the subsequent course of this group precipitated the present study.

STUDY

Ninety-seven patients with hemoptysis of undetermined origin were studied between Jan. 1, 1950, and April 15, 1959. The composition of this group by age and sex is shown in Table II. Only one Negro patient, a 50-year-old woman who has been lost to follow-up, was present in the series and this is considerably

TABLE II. COMPOSITION OF SERIES

	AGE GROUP						
	20-29	30-39	40-49	50-59	60-69	70-79	
Male	2	11	21	17	13	3	
Female	1	5	9	9	5	1	
Total	3	16	30	26	18	4	97

below the usual proportion in our practice—its significance is questionable. The ratio of 67 males to 30 females is in agreement with that noted in most reports. It will be noted that the highest incidence in both males and females was in the decade 40 to 50 and that the age group 40-60 accounted for over one half the patients of both sexes.

The present status of 81 of the 97 patients (83.5 per cent follow-up) was determined as of April, 1960, by means of personal contact, consultation with the referring physician, or by direct mail query. The composition of the group followed is shown in Table III.

TABLE III. FOLLOW-UP

	FOLLOW-UP (YEARS)					PER CENT FOLLOW-UP
	1-3	3-5	5-7	7-9	9-10	
Male						
No. of patients	22	15	16	7	7	
No. followed	21	12	13	6	5	85
Female						
No. of patients	7	5	11	6	1	
No. followed	7	4	7	5	1	80
Total number of patients	29	20	27	13	8	
Total % followed	96.5	80	74	84	75	83.5

It will be noted that 44 patients were followed for periods ranging from 1 to 5 years while 37 were followed for intervals ranging from 5 to 10 years. We attach particular significance to the 96.5 per cent follow-up in the first 3 years after study since one might reasonably expect that carcinoma or tuberculosis, if related to the hemoptysis, should become clinically apparent in this interval.

CLINICAL INVESTIGATION OF THE HEMOPTYSIS

In the initial examination all patients had a bronchoscopy, bronchogram, and culture of the bronchial aspirate for tubercle bacilli. Sixty-nine of the 97 patients had study of the bronchial aspirate for malignant cells and 65 of these were reported negative. Of the remainder, 2 patients with a questionable smear are alive and well 1½ and 6 years later. A 33-year-old male had a report of "malignant smear"—4 years and 7 months later he had resection of a squamous cell carcinoma of the lip but his chest remains normal 5 years after the original report. One questionably malignant smear was reported in 1951 on a 54-year-old male with severe hypertension. He has been lost to the series and his present status is unknown.

Three patients had repeat negative bronchoscopies on occurrence of subsequent hemoptysis. Two patients had angiocardiography and 1 of these also had cardiac catheterization. One other patient had catheterization on a subsequent admission for recurrent hemoptysis.

One 64-year-old male had left exploratory thoracotomy in 1953 because of an equivocal hilar shadow, the nature of which could not be determined by laminography and angiocardiography. The shadow proved to be vascular in origin. Over 6 years later, he is alive and well, without recurrence of hemoptysis.

INITIAL EXTENT AND SUBSEQUENT RECURRENCE OF HEMOPTYSIS

Twenty of the patients (20.6 per cent of the series) presented with streaking (Table IV), whereas 77 (79.4 per cent of the series) were classified as having gross hemoptysis (Table V) varying from ½ teaspoonful to such an extent that one man required multiple transfusions.

TABLE IV. STREAKING

	MALES		FEMALES	
No prior episodes	13			1
Prior episodes		5	1	
Subsequent episodes	3	1	0	0
Lost to follow-up	0	0	0	0
Totals	18		2	

TABLE V. GROSS BLEEDING

	MALES		FEMALES	
No prior episodes	31		15	
Prior episodes		18		13
Subsequent episodes	1	4	2	2
Lost to follow-up	6	4	4	2
Totals	49		28	

It has been suggested that if the hemoptysis is recurrent one must suspect serious underlying disease. Reference to Tables IV and V will reveal that 37 patients either had episodes of hemoptysis extending over a period longer than

6 months prior to examination or subsequently bled at intervals over a period longer than 6 months after examination. Of this latter group, within 3 years, 3 patients showed evidence of serious vascular disease as an explanation of the bleeding. These will be analyzed in detail.

CASE 1.—H. R., a 39-year-old woman, was first seen in March, 1955, with a complaint of intermittent gross hemoptysis over a period of 12 years. Initial examinations, including angiocardiography, were negative. Three years later, in March, 1958, she was readmitted to the hospital because of recurrent increasing bleeding. Two attempts at cardiac catheterization were incomplete because of reactions during the course of the procedure. It was the opinion of the cardiologist, however, that she probably warranted exploration of the mitral valve. This was performed in July, 1958, with no evidence of mitral stenosis. A lung biopsy was taken at the same time and the final diagnosis was primary pulmonary hypertension. She is alive but continues to have episodes of hemoptysis at the present time.

CASE 2.—H. B., a 57-year-old white woman, was first seen in May, 1955, with a history of several episodes of gross hemoptysis in the preceding 18 months. Examination, including esophagoscopy, was negative. During the following 3 years she continued to have isolated episodes of gross hemoptysis, developed obvious signs of congestive failure, and is alive but in a deteriorating condition at the present time.

CASE 3.—K. B., a 40-year-old white man, was first seen in June, 1951, with a history of recurrent gross hemoptysis of 1 year's duration. Initial investigation was negative. Two years later he was readmitted because of recurrent bleeding. Cardiac catheterization proved this to be on the basis of mitral stenosis but operation was refused. He is alive with a grossly enlarged heart and in rapidly deteriorating condition.

In addition, one female (Case 4) continued to bleed intermittently following study and died 15 months later.

CASE 4.—M. D., a 54-year-old white woman, was first seen in November, 1958, with a complaint of gross hemoptysis of several days' duration. Investigation revealed no abnormalities. In June, 1959, she had another episode of gross hemoptysis. Repeat roentgenograms showed no abnormalities and no change. She was readmitted in February, 1960, in shock and died a few days later of a dissecting thoracic aortic aneurysm. There was no hemoptysis during the terminal episode and autopsy revealed no anatomic cause for the previous hemoptyses. Available evidence would indicate that they were isolated and unrelated phenomena.

In addition to the death reported above, 3 other patients are known to be dead—all of causes unrelated to the hemoptysis.

CASE 5.—A 63-year-old white man died 3 years after study from hemorrhage from the renal pedicle after a nephrectomy.

CASE 6.—A 58-year-old white man died 5½ years later from the last of three myocardial infarctions which had occurred in the succeeding years.

CASE 7.—A 52-year-old white man died, 21 months after study, from cirrhosis of the liver.

Patients still alive but with serious disease which has no apparent relation to the hemoptysis include: (a) a 33-year-old man, previously mentioned, who developed squamous cell carcinoma of the lip 4 years later; (b) a 42-year-old man who developed myocardial infarction 14 months later; (c) a 46-year-old woman who became psychotic 5 years later; (d) a 61-year-old man, a hypertensive, who developed a stroke 6 months later and a myocardial infarction

12 months later; (e) a 60-year-old man who developed carcinoma of the soft palate 18 months later; and (f) a 52-year-old man who has had two myocardial infarctions in the 9 years subsequent to study.

ANALYSIS OF THE VARIOUS THEORIES OFFERED TO EXPLAIN HEMOPTYSIS OF UNDETERMINED ORIGIN

1. *Mucosal Ulceration Beyond the Vision of the Bronchoscopist.*—

2. *Undetected Bronchiectasis of a Single Radicle.*—

We feel that it is impossible to either prove or disprove either of the above as the cause of the hemoptysis.

3. *Pulmonary Hypertension.*—Three patients in this group ultimately had their hemoptysis explained on this basis.

4. *Systemic Hypertension.*—Nine patients of the original 97 had systemic hypertension. One 54-year-old man has been lost to the series. The remaining 8 are alive and have not subsequently bled over intervals ranging from 18 months to 8 years.

5. *Blood Dyscrasias.*—There were no blood dyscrasias in this series.

6. *Small Infarct Without X-ray Evidence.*—This is impossible to prove or disprove. However, it strains the imagination to conceive that the many patients in this series who had multiple episodes of hemoptysis would never show x-ray evidence.

7. *Vicarious Menstruation.*—We are convinced of the existence of this syndrome and have seen it occur in other patients with a pulmonary lesion. There were no cases in this series, however, which met the criteria.

8. *Varicosities About the Carina and Upper Lobe Orifices.*—Smidt has ventured the opinion that a probable site of predilection for hemoptysis exists around the carina and upper lobe orifices. He feels that, even in normal individuals, there are often phlebectases in these sites just as there are on the nasal septum. We have not been impressed with these findings in our practice.

SUMMARY AND CONCLUSIONS

Ninety-seven patients with hemoptysis of undetermined origin were examined over a period of 9⅓ years.

Eighty-one of the above group (83.5 per cent) have been followed for periods ranging from 1 to 10 years.

Four of the 81 patients are known to be dead of causes unrelated to the hemoptysis.

Seventy-seven of the 81 patients followed (95 per cent) are known to be living at the present time.

Three of the known living patients, within 3 years of the original examination, had the bleeding explained on the basis of mitral stenosis, congestive failure, or primary pulmonary hypertension.

Although no cases of pulmonary carcinoma or tuberculosis are known to have subsequently developed in this series, it is probably a wise precaution to

re-examine by x-ray all patients at intervals of a few months for 1 year after the original examination. Subsequent episodes of hemoptysis may require repetition of portions of the original study, although our experience would indicate that investigation of the pulmonary artery pressures might prove more productive.

The great majority (91.3 per cent) will continue in good health even though over 10 per cent may continue to have occasional episodes of hemoptysis. In an analogous situation in the urinary tract, with the same prognosis, the term "essential hematuria" is widely accepted. We feel there is equal evidence to support the terminology of "essential hemoptysis" in the cases under discussion.

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Discussion

DR. RODOLFO HERRERA, Guatemala City, Guatemala.—There is a disease called endemic hemoptysis or paragonimiasis which is quite common in Asia. Besides the fact that it was first discovered in a tiger in Amsterdam in 1877 there are two interesting things about this disease, which is caused by a fluke, *Paragonimus westermani*.

First is the fact that it has been reported in some parts of Latin America and in North America in United States Naval personnel. Second is the fact that the larvae of this parasite pass through the duodenal wall and then through the diaphragm and into the lungs, where they give rise to bloody sputum.

Similar life cycles exist in other more common parasites, such as Ascaris, Uncinaria, and the larvae are occasionally found in the sputum. The chest roentgenogram is usually negative at the time of the first bloody sputum, although a few days later it may show minimal areas of soft density which disappear spontaneously very rapidly. This is sometimes called tropical pulmonary eosinophilia in the English literature.

The point which I want to make is that in order to pin the diagnosis of idiopathic hemoptysis on a patient we should probably have negative studies of sputum and stool in search for parasites, in addition to the list of negatives given by Drs. Barrett and Tuttle in their very interesting paper.

DR. R. LEONARD KEMLER, Hartford, Conn.—To confirm the second point in Dr. Barrett's paper, we have had occasion to study a patient over a period of 22 years. This girl was a student nurse at the time when hemoptysis first occurred, and she had, in the 22-year period, a total of ten bronchoscopy studies done by various examiners, as well as twelve bronchograms. At no time was the etiology of the hemoptysis determined. The patient was offered a middle lobectomy 2 years ago, following bronchoscopy which showed

blood coming from the right middle lobe orifice. She refused. One year ago, after the twelfth bronchogram was made, definite bronchiectasis was evident, this time in the right middle lobe, and the patient has had a right middle lobectomy in the past year.

The pathologic examination definitely proved the bronchiectasis in the right middle lobe.

DR. DUANE CARR, Memphis, Tenn.—There is one entity particularly prevalent in our section of the country for which one might well be on the lookout, and that is the broncholith, or bronchial stone. In an area in which histoplasmosis is endemic, there are a great many calcified nodes that are closely associated with the trachea and bronchial tree, including the almost uniformly demonstrable azygos node, as we call it, at the right side of the trachea. In time these may erode into a bronchus and may be expectorated, often being accompanied by hemoptysis for which no other cause can be found.

Obtaining the history of these is somewhat amusing at times. These patients frequently will recall, if prodded, that they indeed spat up what they thought was a piece of a tooth filling or a grain of sand, but not finding any absent fillings, they dismissed it from their minds. You have the diagnosis immediately from the history alone.

Some bronchial stones, or casts, actually form within the bronchi themselves as a result of long-standing inspissated pus, which becomes so dry and so hard that it finally calcifies and forms actual casts of the tracheobronchial tree or segments of it. These you find as staghorn stones, very much like those one finds in the pelvis of the kidney. Sometimes they can be seen at bronchoscopy. When not visible by bronchoscopy, it is not unknown to be able to spot them by careful perusal of serial x-ray films.

It is just one more entity to remove from those that one must designate as "hemoptysis, cause unknown."

DR. THEODORE R. HUDSON, Chicago, Ill.—Dr. Barrett showed one slide in which the presence of varicosities about the upper lobe orifices had been hypothecated. I can verify this in the case of a young woman who had a violent hemoptysis, and in the orifice of the left upper lobe I could see on bronchoscopy a wormlike, glistening mass which pulsated. I couldn't believe my senses, and I bronchoscoped her 2 weeks later with 2 other people present to look in with me. The same thing was seen again, looking just the same as it had before.

This was a varicosity, as shown by removal of the left upper lobe. This paper gives me a nice new term to put on the insurance forms. I am sure that the insurance people will accept "essential hemoptysis" more readily than they will "hemoptysis, etiology undetermined."

DR. TUTTLE (Closing).—I had nothing much to do with this paper, except that I bronchoscoped a number of these patients, and I coined the term "essential hemoptysis." Dr. Barrett is to be credited with all of the work, which was prodigious. We sent out many follow-up letters and called many physicians in order to accomplish this study.

I think it is interesting that relatively few of these patients developed carcinoma. In fact, none in this series did, although there was 1 in the previous group that did after a period of two years. I think that we must not release this to the internists, because if we do, we will miss many carcinomas, and I think that is the one essential fact that must be brought out—that when bleeding occurs, bleeding should be traced, just as it is in the kidney.

The term "essential hematuria" has been known for many years. It was known when I was a student, and that was many years ago, and it is still known. And now we have recoined it for this phenomenon which occurs in the lung. But we still must trace it down, and so I would say on this whole subject, "Carry on, stout fellows!"

LIGATION AND DIVISION OF THE BRONCHUS IN THE SURGICAL TREATMENT OF CAVITARY TUBERCULOSIS

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AUTO-OCCLUSION of the bronchus occurs in the natural course of tuberculosis as an inconstant but very fortunate event. Many provocative concepts have been offered on its significance in cavity healing. Sudden and dramatic cavity closure occurred in unpredictable ways under the influence of pneumothorax, thoracoplasty, and even phrenic nerve paralysis. The credit that belonged to bronchial occlusion as the essential common denominator among these successful cases was bestowed liberally upon the various collapse measures by their enthusiastic proponents.

The importance of bronchial occlusion became obscured in later years with the popularity of resection therapy for pulmonary tuberculosis and, while accepted modern concepts of treatment have proved adequate for the vast majority of patients, there remains a significant group of patients for whom no surgical solution exists.

The purpose of this presentation is to record our experiences with 25 cases of advanced cavitary tuberculosis treated by operative bronchial occlusion.

HISTORICAL BACKGROUND

Anatomic, Bacteriologic, and Pathophysiologic Concepts.—

The concept of operative occlusion of the draining bronchus in cavitary tuberculosis evolved from basic studies on atelectasis. Clinical observations on ateletasis in tuberculous lungs and investigations on the behavior of tuberculous cavities and the role of their draining bronchi provide fundamentals essential to the logic of our thesis. Extensive bibliographies on the study of atelectasis have been compiled by many authors, notably by Coryllos[20] and Churchill.[20a] Selected references have been made to these and other studies, as they applied particularly to the development of operative bronchial occlusion in the treatment of tuberculous cavities.

The clinical acceptance of concepts developed experimentally frequently must await emotional or technical advances. In 1844 Mendelssohn[1] showed experimentally that bronchial obstruction caused atelectasis, and in 1879 Lichtheim[2] occluded bronchi in rabbits with sticks of lamenaria and stressed not only the importance of bronchial obstruction in lung collapse but also the role of the blood in the absorption of air distal to bronchial obstruction.

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Nevertheless, numerous theories on atelectasis continued to appear in the literature. Elliott and Dingley[3] in 1914 challenged the widely accepted concept of W. Pasteur[4, 5] in England that paralysis of the intercostal muscles and diaphragm was primary in the cause of atelectasis and pneumonia. These authors recognized that bronchial obstruction by retained secretions caused atelectasis and recommended cough and expectorants in its treatment. The wisdom of this concept became obvious clinically only after the adoption of bronchoscopic aspiration in the late 1920's. In 1928 Lee and his associates[6] presented very convincing experimental proof of the obstruction theory of atelectasis.

The popularity of pneumothorax and thoracoplasty in the 1920's aroused much interest in the possible effects on tuberculosis of spontaneous or induced atelectasis. An experimental approach to the pathophysiology of therapeutic pneumothorax by Andrus[7] in 1925 involved the collapse of one lung in dogs by bronchial ligation. The microscopic appearance of the lung after several months was one of passive vascular congestion and a dense cellular stroma which seemed to be composed of alveolar cells and many fibroblasts. During the same year, Gardner[8] reported on the pathology of artificial pneumothorax in tuberculosis. He observed that fibrosis in collapsed tuberculous lung was greatly in excess of that in an uncompressed tuberculous lung and suggested that the fibrosis might be accelerated or stimulated by lymph stasis. More important than this to our present thesis, he made reference to the failure of miliary tuberculosis in man to localize in collapsed lung tissue.

Van Allen and Lindskog[9] in 1930 contributed basic understanding to the mechanics of atelectasis with their discovery of intralobar collateral ventilation in dogs. They showed that atelectasis occurred when lobar bronchi were occluded, whereas atelectasis failed to occur when the occlusion was at the segmental level in otherwise normal lungs. Collateral ventilation was found to be present in normal respiration, being a delicate mechanism activated by a pressure differential of only a few millimeters of water. The presence of collateral ventilation in human lungs was confirmed in 1948 by Baarsma.[10] Van Allen[11] reported further in 1932 that patchy or lobular atelectasis will follow obstruction of small bronchi, provided that collateral ventilation has been suppressed by previous inflammatory thickening of the alveolar septa. An additional feature of collateral ventilation was provided in 1931 by Adams and Livingstone,[12] when they discovered that collateral ventilation occurred between lobes when interlobar fissures were not complete. The importance of this finding to bronchial ligation will be discussed later.

Phthisiologists presented divided opinions on the effects of atelectasis on pulmonary tuberculosis. Some observed deleterious effects while others considered atelectasis to be beneficial. Habliston[13] in 1928 cited the marked increase in negative intrapleural pressure following massive lung collapse and recommended artificial pneumothorax to relieve the resultant cardiac displacement and associated symptoms. Jacobaeus and Westermark[14] in 1930 and E. E. Glenn[15] in 1931 reported on the deleterious effects of atelectasis. The latter author noted that, following lobar atelectasis, cavities sometimes re-opened in ipsilateral lobes, presumably because of the more negative intrapleural pressure. The treatment suggested was artificial pneumothorax.

Favorable clinical effects of atelectasis on the course of pulmonary tuberculosis were described by Packard[16] in 1928, Hennell[17] and Korol[18] in 1931, and by Zavod[19] in 1938. The major contributions by Coryllos and by Adams on this concept will be reviewed.

The exhaustive studies made by Coryllos during the late 1920's and 1930's added greatly to our knowledge of cavitary tuberculosis, especially of the role of the draining bronchi, and the clinical importance of bronchial occlusion and atelectasis. Coryllos and Birnbaum[20] reported in 1928 on obstructive massive atelectasis of the lung, and noted that complete bronchial obstruction or lung compression always was present. They stated that artificial pneumothorax might be palliative, but was not therapeutic, and proposed bronchoscopic aspiration as the treatment of choice. In a later report in 1929, Coryllos[21] described the circulation of atelectatic lung and noted that ischemia was proportionate to the degree of lung collapse, that circulation and ventilation were parallel functions. In studies on pneumonia he observed that the fate of the lung after bronchial obstruction depended upon the

microbes infecting the obstructing mucus,[22] and confirmed earlier work concerning absorption of gases from obstructed parenchyma by the circulating blood.[23]

Coryllos and Ornstein[24] summarized their concepts in 1938. They attempted to correlate pathologic features of the draining bronchi to the seemingly erratic behavior of cavities[25-30]: the usual oblique entry of draining bronchi through the cavity wall favored temporary bronchial obstruction because of compression as the cavity distended; inflammatory changes in the congested bronchial walls and tuberculous destruction of supporting cartilage rings, in the presence of inspissated mucus and blood, permitted temporary bronchial collapse and a check-valve mechanism[31, 32] and set the stage for successful fibrous tissue obliteration and permanent bronchial occlusion and cavity healing; the passive vascular congestion attendant upon subsequent atelectasis resulted in tissue hypoxia, which in turn stimulated fibrous proliferation (likened to Volkmann's ischemic contracture).[33] They postulated that permanent atelectasis, as with thoracoplasty, accounted frequently for successful cavity closure since the proliferation of fibrous tissue in distorted bronchi was stimulated by an ischemic environment and permanent bronchial occlusion occurred, whereas pneumothorax failed frequently to accomplish cavity closure since the maintenance of collapse and ischemia were intermittent. Reference to the stimulating effect of tissue hypoxia on fibrous tissue formation was made in 1930 by Leriche and Policard.[34]

Coryllos and Ornstein included, in their report, studies on the bacteriology of tuberculous cavities. To refute many previous reports of almost universal secondary bacterial contamination, it was possible by careful technique to demonstrate sterility of open cavities, except for the tubercle bacillus. Coryllos had suspected that this was true, since serious suppurative complications had not been observed following cavity closure that occurred spontaneously, or by virtue of imposed collapse measures, such as thoracoplasty. Coryllos concluded: "These bacteriologic findings are of considerable practical importance. In fact, if the danger of obliteration of the draining bronchus is removed, there is no reason why we should not try to obtain it surgically, especially in cavities in which all other means of collapse, including thoracoplasty, have failed."

Simultaneous with the work of Coryllos during the 1930's, W. E. Adams was investigating the effects of bronchial occlusion. Adams, Van Allen, and Livingstone[35] reported on the response of bronchi to thermal injury and to silver nitrate cauterization, and observed the possibility of creating fibrous bronchial occlusion by these methods. A safe and reliable method for closing large bronchi in dogs by endoscopic application of silver nitrate solution was suggested by Adams in 1933.[36] Aware of the beneficial effect of atelectasis on pulmonary tuberculosis, Adams and Vorwald[37] created lobar atelectasis in dogs by this technique and demonstrated, by gross and microscopic examinations, the beneficial effects of atelectasis on miliary tuberculosis, as well as the protective influence of established atelectasis against tubercle bacilli administered intravenously. The effects of atelectasis on tuberculous lesions, produced endobroncially and subpleurally, also were described. In the latter instances bronchial secretions were increased and complete bronchial occlusion with silver nitrate was difficult to accomplish. They reported on the technique applied in 4 human cases in which complete bronchial occlusion was not obtained, apparently because of the copious bronchial secretions. This obstacle to complete bronchial occlusion by cauterization was overcome by Escudero and Adams,[38] in 1938, when they performed bronchial ligation in dogs and accomplished healing of experimental tuberculosis in atelectatic lobes, while the tuberculous lesions progressed in aerating lobes in the same animal. Kawabata[39] reported on the protective effects of induced atelectasis on hematogenous tuberculosis in rabbits in 1938.

The vascular changes caused by induced atelectasis were described by Adams[40] as an increased vascularity, in the nature of a passive congestion rather than an active hyperemia. Fibrous tissue proliferation in the atelectatic lung was considered insignificant in amount compared to the marked degree of fibrosis seen in infected atelectatic lobes. The favorable effects of atelectasis on clinical tuberculosis were reported by Adams and Singer in 1935.[41]

The introduction in the late 1930's of transpleural decompression of cavities, and the interest aroused by investigations in cavitary dynamics, led naturally to a transcavitary attack

on the draining bronchus to effect cavity closure. Coryllos and Ornstein[24] described unsuccessful attempts at transcavitary bronchial occlusion with sclerosing agents, electrocoagulation, and by the implantation of pedunculated muscle. Davidson[42] mentioned the use of a special telescope designed to locate and coagulate the draining bronchus. The various concepts were appealing, but the methods generally were not successful.

The lead provided by Escudero and Adams,[38] in using a direct surgical approach to bronchial occlusion by ligation, apparently was lost in the new popularity of resection therapy, and the untimely death in 1938 of Dr. Coryllos, who was the greatest proponent of this concept. In his monograph published in 1937 on The Surgery of Pulmonary Tuberculosis,[43] Coryllos stated that ". . . the key to the treatment of tuberculosis cavities is not to be looked for in their walls, but in their bronchial outlets. Therefore, our efforts must tend to the definite obiteration of these bronchi. Unfortunatey, notwithstanding persistent research, I have not yet been able to find a procedure by which we could locate our intervention to the closure of these bronchi. Let us hope that we may succeed some day."

Although attempts at direct surgical approach to bronchial occlusion were abandoned for several years, many phthisiologists, familiar with the work of Adams, have tried to accomplish bronchial occlusion endoscopically. The senior author of this report (J. M. C.) was among these and was successful on several occasions in converting bronchial stenosis to temporary bronchial occlusion, with a few eventual good results. In 1940 Crafoord and Frenckner[44] described a successful clinical case of bronchial cauterization with silver nitrate. Their patient had developed bronchiectasis beneath a thoracoplasty and had positive sputum. Revision thoracoplasty was considered to be not appropriate in these circumstances. Although a tiny bronchial opening persisted after cauterization, the sputum converted and the patient remained well 2 years later. Melfi, Schverlich, and Tamborini[45] reported also on the success of endobronchial treatment of pulmonary tuberculosis.

Since the foregoing experiments and conclusions were made in the pre-chemotherapy era, the question arises as to whether pathologic changes have occurred with chemotherapeutic agents that would be significant to operative bronchial occlusion. Auerbach, Katz, and Small[46] reported that stretopmycin induced a process of cavity healing different from that which occurred prior to the use of this drug. Reduction in perifocal reaction, thinner cavity wall, and lining of the bronchocavitary junction with squamous columnar epithelium, which extended for varying distances onto the cavity wall, were the major observations. Auerbach[47] observed that, in the era before chemotherapy, "closed healing" was by far the most frequent mechanism of cavity closure, occurring as the result of apposition of granulating surfaces of the ulcerated bronchus at the bronchocavitary junction, with eventual fibrous obliteration. Under the influence of chemotherapy, "open healing" occurred more frequently, with cavity inspissation and re-epithelialization and continued patency of the bronchocavitary junction. Thompson[48] reported 9.6 per cent incidence of "open healing."

The implications of these findings convey importance to studies on the pathogenicity of tubercle bacilli remaining in inspissated cavities. The respiratory metabolism of the tubercle bacillus in inspissated cavities had been studied by Novy and Soule[49] in 1925, and by Loebel, Shorr, and Richardson[50] in 1930. D'Esopo[51, 52] reported in recent years that such organisms were nonviable in 85 to 95 per cent of resected lesions and stated that there is no general agreement that these bacilli are, in fact, dead. The tuberculostatic or tuberculocidal influence of acidic necrotic debris in inspissated cavities was the subject of similar investigations by Dubos.[53] From the practical standpoint, ligation and division of the draining bronchus produces an unfavorable environment for the tubercle bacillus by causing tissue hypoxia and by retaining toxic necrotic debris within cavities.

The blood flow in dog lungs, made atelectatic by bronchial ligation, was reported by Björk and Salen[54] in 1950. Blood flow through the atelectatic lung decreased progressively during the first month, until practically no blood passed through. Peripheral arterial desaturation was present immediately and returned gradually to normal as the blood flow reduced in the collapsed lung. No decrease in size of the pulmonary artery was noted. The vascular block was presumed to be in the capillary bed.

Whereas the report of Björk and Salen deals with atelectasis and tissue hypoxia, factors considered beneficial sequelae of bronchial ligation, Hanlon, Scott, and Olsen

and their co-workers[55] reported on the deleterious effects on experimental tuberculosis of pulmonary artery ligation. The mechanism of enhanced growth of tubercle bacilli under these circumstances lies in the fact that such lungs become perfused with highly oxygenated systemic blood through enlarged bronchial arteries. In a negative sense, therefore, these studies substantiate the virtues of bronchial ligation and division in the treatment of pulmonary tuberculosis. Further reference to ligation of segmental branches of the pulmonary artery will be made in our discussion.

Concepts on bronchial occlusion, similar to those developed in this country, received passing attention almost simultaneously in Europe. Jacquerod[57] in France, on the basis of his studies on tuberculous cavities, voiced the later conclusions of Coryllos, when he stated in 1924 that "when surgeons are able to accomplish permanent closure of the draining bronchus, the problem of closure of tuberculous cavities will be solved."

Nissen and Lezius, when assistants of Sauerbruch in Germany, succeeded in 1932 in occluding bronchi in dogs and observed that the lung was transformed to a fibrous mass after 3 months.[57] Twenty years later, the same two surgeons reported in Germany on bronchial ligation and division in 16 clinical cases of advanced cavitary tuberculosis.[58] Their conclusions on selection of patients, operative technique, various essential precautions and clinical results, are very comparable to our own conclusions, arrived at without knowledge of their work. In his excellent book on lung resection, published in 1953, Lezius[59] devoted a short section to bronchial ligation and division, with operative technique and important bronchocavitary anatomy beautifully illustrated.

Bogush, in Russia, impressed with the results of Nissen and Lezius, began to perform ligation and division of the bronchus in 1953. By 1957, he and his associates were able to report excellent results in 50 clinical cases of advanced cavitary tuberculosis.[60, 61] Conversion of sputum and cavity closure occurred in 43 patients, cavities remained open in 5 patients, and 2 patients died with contralateral pneumonia. The general conclusions of this report also are in agreement with our own. Margulis[62] reported in Russia, in 1957, on successful control of hemorrhage from a cavity by bronchial ligation and division in a patient who could not have tolerated more extensive methods of treatment. A similar case will be described in this presentation.

The American medical literature to our knowledge contains no previous report on bronchial ligation and division in the treatment of cavitary tuberculosis. The 25 cases to be presented comprise our total experience with this operation, the first having been performed in 1948.

SELECTION OF CASES

The decision to perform bronchial ligation and division was made most often on the basis of a combination of unfavorable features of cavitary tuberculosis. Many patients in this group obviously were beyond consideration for standard resection and collapse procedures. These had multiple cavities involving one or more lobes, often bilaterally, and over the years had healed diffuse parenchymal disease, now inconspicuous, at the expense of much functioning lung tissue. Several were thoracoplasty or pneumothorax failures, sometimes having been complicated by bronchopleural fistula and empyema. Marked reduction in pulmonary function and organism resistance to the major chemotherapeutic drugs were constant features of this group of tubercular relics, several of whom are present in every sanatorium, preparing to succumb eventually to their disease.

The group of patients just described comprised 15 of our 25 cases. Five among these were considered preoperatively to be suitable candidates for resection and thoracoplasty procedures. At operation the decision was made to

perform ligation and division of the bronchus when the true extent of the disease process became apparent, and the concept of the proposed operation became untenable. For example, when the proposed operation for cavitary disease was upper lobectomy, superior segmental resection of the lower lobe and thoracoplasty, and extensive fibronodular disease was discovered in the middle and basilar segments, the proposed operation then assumed a high complication risk that was unacceptable to these patients. Pneumonectomy for them was unsuitable because of contralateral cavitary disease, or a functionally inadequate lung. Thoracoplasty, to be successful, would have had to be extensive and too demanding on pulmonary function. The surgical alternative for these patients was to subject them to an unreasonable risk, or to abandon hope and do nothing.

Three patients not included in this category, although similar in clinical features, were subjected to ligation and division of the bronchus as "desperation measures" (Cases 3, 10, and 12). They survived postoperatively 1 month, 2 months, and 2 months, respectively. We considered it as unlikely that the operations altered the inexorable courses of their disease.

Ligation and division of the bronchus was performed on three occasions when the proposed resection could not technically be accomplished. In Cases 1 and 4, right upper lobectomy beneath a thoracoplasty was attempted. These carnified lobes were fused to the chest wall and to adjacent lobes. The organized and calcified tissues surrounding the hilar vessels defied dissection and identification. The bronchus in each case was secured with great difficulty, and was ligated in 1 case and divided in the other. Case 7 also was proposed for a right upper lobectomy for control of hemorrhage from inactive tuberculous bronchiectasis and calcification. Uncontrollable bleeding was encountered wherever the dissection was directed to mobilize the adherent lobe. The hilar structures therefore were approached posteriorly and the posterior segmental bronchus was ligated and divided. The pulmonary hemorrhage was controlled completely by this maneuver.

Two female patients became candidates simultaneously for bronchial ligation and division when one refused resection beneath a left thoracoplasty, and the other refused a thoracoplasty that would have been essential following the recommended right upper lobectomy (Cases 13 and 14). Each consented to the proposal of ligation and division. Operated upon the same day, each had an excellent clinical result.

Case 6 was unique in that the cavitary left lung contained extensive fibrosis, the result of radiation therapy following radical mastectomy for breast carcinoma. Upper lobectomy, superior segmental resection, and extensive thoracoplasty were considered hazardous and too demanding upon the markedly reduced pulmonary function. Old contralateral disease precluded pneumonectomy. The upper lobe and superior segmental bronchi were divided and a small posterior thoracoplasty was performed. An excellent result has extended almost 4 years to date.

The operative indications were debatable, in our opinions, only in Case 22. Bilateral upper lobectomy and thoracoplasty could have been justified for this patient. Realizing that there were multiple cavities in both upper lobes and scattered infiltrative and nodular disease in both lower lobe apices, we were concerned with avoiding space problems and preserving maximum pulmonary function. The unexpected and unfortunate outcome in this case remains unexplained.

The factor of age was not an important indication in this series of cases, except in Cases 17 and 25. These patients were 66 and 75 years of age but, in spite of drug resistance, might have tolerated resection. The operative trauma and the potential complications were considered to be less with bronchial ligation and division. Similar reasoning might be applied to patients having cavitary tuberculosis, who have had relatively recent operations for carcinoma, with doubtful outcome. Psychotic patients incapable of cooperation, in whom immediate bacteriologic negativity is an important safeguard to other patients and personnel, logically are candidates also for this operation.

Experience gained from the diverse problems encountered in this series of 25 cases has enabled us to formulate certain rules and precautions in case selection, as well as in operative technique. For this reason we considered it essential to present each case in some detail, along with diagrams of representative roentgenograms of the chest.

CASE REPORTS

CASE 1.—(Fig. 1; P. O., 50, white male.) Onset 1943, with far-advanced disease in all lobes. Two-stage thoracoplasty in 1947 failed to close giant cavity. Upper lobectomy was planned. Bronchus to RUL ligated, when at thoracotomy on Sept. 11, 1948, a pneumonectomy was the only alternative. Operation successful. Death occurred 6 weeks later from amyloid uremia.

Comment: Successful. This first case of bronchial ligation accomplished cavity obliteration and sputum conversion. The bronchus should have been divided. Death unrelated to operation.

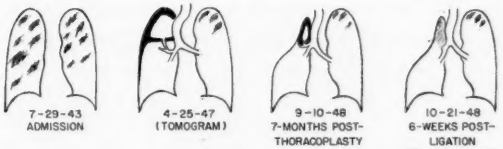

Fig. 1.

CASE 2.—(Fig. 2; M. C., 40, white female.) Onset 1942, bilateral apical. Cavities RUL, LUL, and superior segment LLL in 1952, with drug resistance and pulmonary insufficiency. At operation on April 22, 1953, left upper lobectomy, superior segmental resection, and thoracoplasty was considered too hazardous. LUL bronchus divided, found to be completely occluded. Superior segmental bronchus and accessory subapical bronchus divided (see Fig. 29). Extraperiosteal Gelfoam plombage, ribs 1-4. Remains well after 7 years.

Comment: Successful. Auto-occlusion of LUL bronchus and accessory sub-superior segment were interesting features of this case. The latter was divided along with the superior segment, possibly discouraging collateral ventilation.

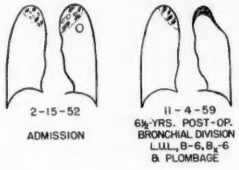

Fig. 2.

CASE 3.—(Fig. 3; M. K., 31, white female.) Onset 1941. Bilateral pneumothorax failed to close cavities in RUL and superior segment of RLL. Presented for surgery in 1953 as "desperation measure" with increasing parenchymal disease, bilobar cavities on right, drug resistance, uncontrolled fever to 103° F. daily, and marked ventilatory impairment. Cavity entered inadvertently, closed. Bronchopleural fistula and empyema fatal after 1 month.

Comment: Failure. Lung should have been mobilized in extraperiosteal plane over area of disease. We did not consider the complication to be condemning to operation performed on this patient with fulminating disease.

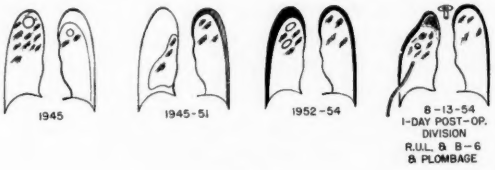

Fig. 3.

CASE 4.—(Fig. 4; K. W., 48, white female.) Onset 1949, with disease in all lobes, and a large cavity in a contracted RUL, persisting after 2 years of pneumothorax, and after plombage and thoracoplasty. Carnification of RUL and hilar structures defied resection on Nov. 6, 1954. RUL bronchus divided, as only alternative. Sputum converted. Remains well.

Comment: Successful case which demonstrates that the difficulties encountered in performing resection for thoracoplasty failure can be solved by bronchial ligation and division.

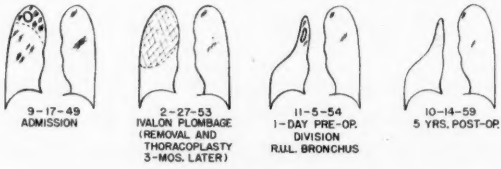

Fig. 4.

CASE 5.—(Fig. 5; J. B., 41, white female.) Onset 1946, remission to 1950, when all lobes involved. Pneumothorax failure on right, controlled by thoracoplasty. Cavity developed in superior segment, LLL, and segmental resection planned. At operation on March

14, 1956, extension of disease into basilar segments indicated hazardous situation for segmental resection. Two divisions of B-6 divided. Sputa intermittently positive for 1 year, negative since then.

Comment: Eventual successful case. The entire superior segmental bronchus should have been divided. Cavity control could not be claimed for operation performed. Subsegmental bronchial ligation is ineffectual.

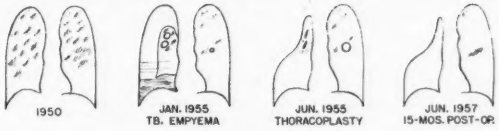

Fig. 5.

CASE 6.—(Fig. 6; M. L., 37, white female.) Onset 1936, with cavities RUL, LUL, lingula, and superior segment of LLL. All cavities closed after 4 years bilateral pneumothorax. Left radical mastectomy for breast carcinoma in 1954, followed by chest wall x-radiation. Cavities reopened LUL and LLL in 1955. Drug resistance, borderline pulmonary function, and contralateral disease indicated bronchial division. Operation on May 24, 1958. Sputa converted. Remains well.

Comment: Successful. Application of this operation to patients with recent carcinoma and radiation fibrosis is recommended.

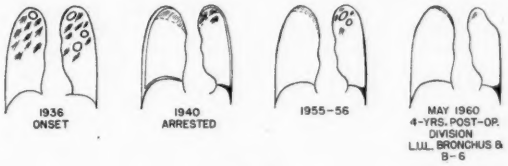

Fig. 6.

CASE 7.—(Fig. 7; G. A., 59, white male.) Stable, honeycombed disease RUL many years. Repeated hemoptyses late 1956-1957. Sputum negative. Hemogram normal. Lobectomy attempted on May 16, 1957. Lobe carnified; bleeding profuse. Posterior segmental bronchus led to major disease and was divided. Bleeding controlled. Unexpected degree of collapse indicated no collateral ventilation. Remained well 6 months, then died with acute leukemia.

Comment: Successful case which demonstrates application of bronchial division for pulmonary bleeding and to retrieve a technically difficult dissection problem.

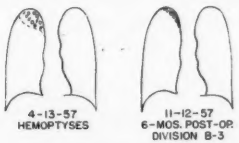

Fig. 7.

CASE 8.—(Fig. 8; Z. V., 23, white female.) Onset Puerto Rico 1951. Exacerbated in 1953. Presented in 1957 in New York City with cavities RUL, LUL, and LLL, and drug resistance. Planned bilateral resections and thoracoplasty. At operation on Aug. 16, 1957,

extensive basilar disease indicated bronchial division as safer procedure. LUL and B-6 divided. RUL resected on Sept. 27, 1957. Remains well.

Comment: Successful case which demonstrates the change of operative plan upon discovering unexpected extent of disease, and use of bronchial division when pneumonectomy is contraindicated. Today we would perform also a selective extraperiosteal thoracoplasty.

Fig. 8.

CASE 9.—(Fig. 9; F. P., 45, Negro female.) Psychotic, syphilitic Negro woman developed bilateral disease in 1949. RUL resected 1954. Cavity in basilar segments of RLL in 1956. Left sanatorium against medical advice in 1957, returned 1958 with enlarged cavity, drug-resistant organisms, low pulmonary function. Bronchial division considered procedure of choice. At operation on April 11, 1958, cavity opened, filled with saline, and "bubbled" by anesthetist to identify communicating bronchi. B-9 and B-10 divided. Cavity remained open and bronchiectasis developed. Completion pneumonectomy in October, 1958.

Comment: Failure. Deliberate opening of the cavity to identify draining bronchi probably should not be done. We do not believe that basilar cavities are best treated by bronchial division, especially in the presence of lung distention following ipsilateral lobectomy.

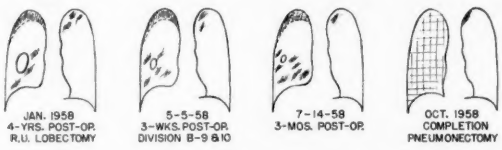

Fig. 9.

CASE 10.—(Fig. 10; W. J., 40, white male.) Onset right apical disease in 1943. Disciplinary problem, failed to curtail activities and to take drugs. Accepted hospitalization in 1957, with RUL, LUL and LLL cavities, and old empyema, right. Organisms resistant. Thoracoplasty June, 1957. Marked impairment of pulmonary function. LUL bronchus and B-6 divided on April 16, 1958, as "desperation measure." Cavities closed and sputum converted. Cardiopulmonary failure was progressive and death occurred 10 weeks postoperative.

Comment: Failure. Successful cavity collapse was accomplished. We did not consider that the operation performed was responsible for death.

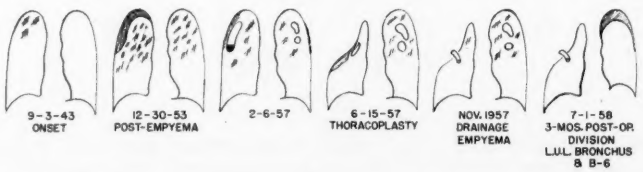

Fig. 10.

CASE 11.—(Fig. 11; A. R., 35, white female.) Onset LUL disease Puerto Rico 1950, improved after 1 year of pneumothorax and triple chemotherapy. Presented in New York City in 1956 with extensive disease, and cavities in RUL, RLL and LUL. Organisms resistant. Pulmonary function markedly reduced. Presented for surgical evaluation in 1958; bronchial division considered procedure of choice. On April 24, 1958, RUL bronchus divided. Lower lobe cavity extended into basilar segments. Cavity opened, filled with saline, and "bubbled" by anesthetist. B-6 and B-9 divided. RUL continues to ventilate, and both cavities remain open to present time. Opportunity still present for plombage or resection.

Comment: Failure. Demonstrates the virtues of simultaneous extraperiosteal thoracoplasty, as portrayed in Fig. 26. This should have been done in this case to obliterate channels of collateral ventilation. Probably B-10 should also have been divided.

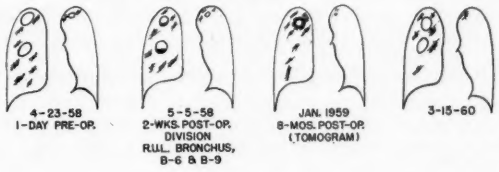

Fig. 11.

CASE 12.—(Fig. 12; M. P., 56, white male.) Syphilitic, diabetic, schizophrenic man, presented in 1952 with extensive bilateral disease. Cavity persisted in RUL. Personality precluded cooperation. Steady deterioration. Organism resistance by 1958. Bronchial division considered only possibility to retrieve desperate situation. RUL bronchus divided on June 20, 1958. Cavity entered inadvertently in extrapleural plane; closure with absorbable sutures. Proximal bronchial stump disrupted on fourth postoperative day. Empyema drained. Death unexpected on Aug. 30, 1958. Autopsy showed perforated gall bladder, general peritonitis, adequately drained empyema.

Comment: Failure. Lung mobilization should have been done in the extraperiosteal plane to avoid entering the cavity and to provide lateral collapse. In addition to operative complications, death was related to ruptured gall bladder and peritonitis.

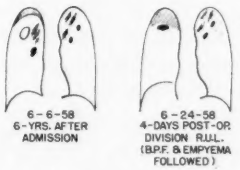

Fig. 12.

CASE 13.—(Fig. 13; H. F., 52, white female.) Chronic alcoholic. Small RUL cavity in 1949. Two large cavities by 1950. Thoracoplasty refused. Cavities closed intermittently. LLL cavity in 1951. Inferior alveolar ridge resected for carcinoma in 1954. Uvula excised for recurrence in 1956. Radical neck dissection in 1957. Meanwhile, cavities persisted. Bilateral resection and thoracoplasty refused. Consented to bronchial ligation and division. RUL and B-6 divided on July 16, 1958. Cavities closed. Superior segmental resection of LLL scheduled for January, 1959. Patient died that month of pulmonary embolus following repair of strangulated inguinal hernia.

Comment: Successful case. Refused resection and thoracoplasty. Death 6 months later was not related to operation.

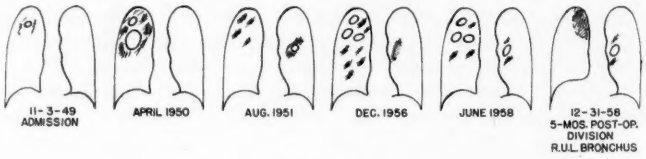

Fig. 13.

CASE 14.—(Fig. 14; E. J., 38, Negro female.) Onset in January, 1955. All lobes involved. Cavities in RUL and LUL, persisting during pneumoperitoneum and chemotherapy. Thoracoplasty on left in October, 1957. RUL resected in January, 1958. Resection beneath thoracoplasty for persistent cavities refused, but consented to bronchial division. LUL bronchus divided on July 16, 1958. Cavities closed and sputum converted. Remains well.

Comment: Successful case. Refused resection beneath thoracoplasty.

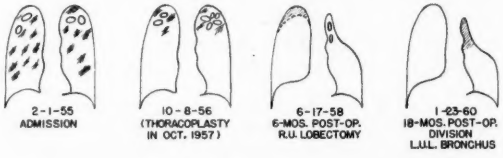

Fig. 14.

CASE 15.—(Fig. 15; W. H., 32, white male.) Minimal tuberculosis in 1944. Exacerbation bilaterally in 1955. Refused hospitalization until 1957. All lobes involved, with cavities in RUL, RLL, LUL, and LLL. RLL cavity closed by January, 1958. Pulmonary function borderline. Upper lobectomies, superior segmental resections, and thoracoplasty, bilaterally, considered too extensive. RUL bronchus divided on July 17, 1958, with effective cavity closure. Left thoracotomy on March 9, 1959. Apical-posterior segmental bronchus of LUL divided. The anterior and lingular segments were very large. To preserve maximum function of these segments, and to prevent or reduce collateral ventilation into the apical-posterior segments that might prevent their collapse, the anterior segmental bronchus was divided (see Fig. 28). B-6 also was divided. Cavities closed and sputum converted. Remains well.

Comment: Successful case of bilateral bronchial ligation and division. Today we would perform simultaneous selective extraperiosteal thoracoplasty, and ligate and divide prophylactically B-6, right, to ensure continued cavity closure in that segment.

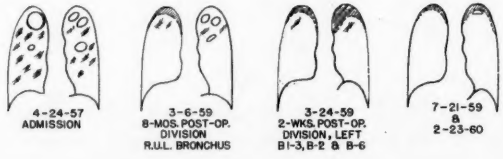

Fig. 15.

CASE 16.—(Fig. 16; W. G., 46, white male.) Onset 1955. Remained hospitalized. Multiple cavities RUL. Giant cavity RLL apex. LUL honeycombed. Sputum persistently positive. MBC, 39 L. per minute. VC, 42 per cent. TVC, 75 per cent in 3 seconds. Right lung performed 14 per cent of total ventilation. Fluoroscopy showed air-trapping in giant

cavity. Arterial O_2 89 per cent breathing room air, and 93 per cent breathing oxygen. RUL bronchus and B-6 divided on Sept. 4, 1958. Sputum converted and has remained negative. Three months later, MBC was 43 L. per minute, and VC 77 per cent. Arterial oxygen saturation normal.

Comment: Successful case which demonstrates improved ventilatory and respiratory function. Today we would perform also a small extraperiosteal thoracoplasty to assist collapse and to discourage collateral ventilation.

Fig. 16.

CASE 17.—(Fig. 17; H. Z., 66, white male.) Onset October, 1956. Exudative disease in all lobes on right. Multiple cavities in RUL. Diaphragms flattened. Organisms resistant to major drugs in 1958. Elected to perform bronchial division because of age, poor pulmonary function, and organism resistance. RUL bronchus divided on May 11, 1959. Cavities closed and sputum converted.

Comment: Successful case, age 66. Advisable to perform simultaneous extraperiosteal thoracoplasty over apex.

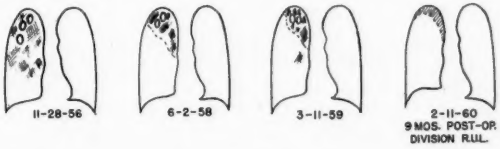

Fig. 17.

CASE 18.—(Fig. 18; H. M., 58, white male.) History of pulmonary emphysema. Onset tuberculosis August, 1957. Dense exudative disease in RUL and apex of RLL. Minimal disease LUL. Some contraction of RUL occurred after 18 months. Ventilatory studies and blood gas analyses confirmed moderate emphysema. RUL bronchus divided on June 8, 1959. Cavities closed and sputum converted. Remains clinically well.

Comment: Successful case. Extraperiosteal thoracoplasty over apex advisable.

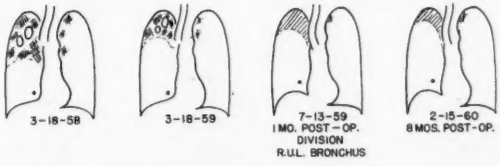

Fig. 18.

CASE 19.—(Fig. 19; W. G., 49, Negro male.) Exudative disease in all lobes in 1954. Cavities persisted in contracted RUL. Left sanatorium against medical advice. Increased disease bilaterally in 1959. Pulmonary function markedly diminished. At operation on Sept. 16, 1959, because of incomplete major fissures and extensive middle lobe and basilar disease,

decision made to divide RUL bronchus and B-6 as alternative to hazardous resection. Posterior thoracoplasty, ribs 2 to 5. Cavities closed. Sputum converted. Remains well.

Comment: Successful case. Not necessary to remove ribs.

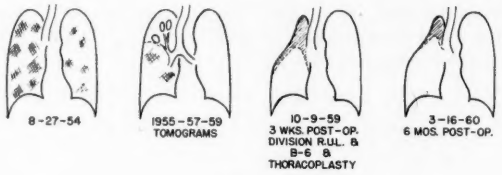

Fig. 19.

CASE 20.—(Fig. 20; E. S., 45, white male.) Onset 1951. Exacerbation 1956. Inadequate chemotherapy on these occasions. Diffuse disease in RUL, with contracted thoracic cage and retracted trachea. Sputum positive October, 1959; cavities in RUL and apex of RLL. Lobectomy and segmental resection planned. At operation, on Oct. 14, 1959, found extensive disease in RML and basilar segments, considered hazardous circumstances for resection. RUL bronchus and B-6 divided. Cavities closed and sputum converted. Discharged from hospital on thirteenth postoperative day. Septic course 3 weeks later, with abundant phlegm containing tubercle bacilli. RML infiltration presumed tuberculous pneumonia. Pneumonectomy was considered when, in January, 1960, the RML cleared, the sputum became nil and negative for tubercle bacilli. Subsequent course excellent.

Comment: Complicated but successful case. Illustrates point to not decide too quickly on basis of bizarre postoperative x-ray signs to accept failure and resort to resection.

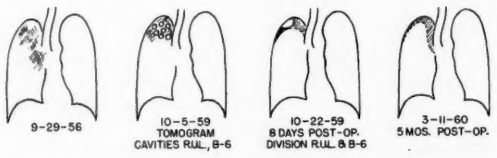

Fig. 20.

CASE 21.—(Fig. 21; V. D., 48, white male.) Onset 1947, all lobes. Two large cavities in LUL remained open following thoracoplasty in 1947. Apical-posterior and anterior segmental resections of LUL on Feb. 14, 1949. Sputum converted. Giant cavity RUL in April, 1958. Drug resistance present by April, 1959, and marked pulmonary insufficiency. Bronchial

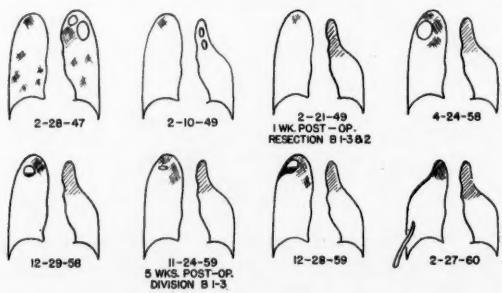

Fig. 21.

division elected as procedure of choice. At operation on Nov. 17, 1959, it was considered essential to preserve the very large anterior segment. The apical-posterior bronchus was divided. To prevent collateral ventilation, an "artificial fissure" was created between the apical-posterior and the anterior segments. Tuberculous empyema developed 5 weeks later, the cavity having ruptured through the "artificial fissure." Drainage and thoracoplasty done. An eventual good result is expected.

Comment: Failure. No attempt should have been made to create an "artificial intersegmental fissure." The lobar bronchus should have been divided and an apical extraperiosteal thoracoplasty performed.

CASE 22.—(Fig. 22; M. N., 48, white female.) Discovered in 1947 to have hyperthyroidism, diabetes mellitus, and LUL tuberculosis. Thyroidectomy done. LUL cleared with chemotherapy but progressed in 1952 when diabetes was uncontrolled. Hemoptyses 1954-1955. Sputum positive 1957. Extensive parenchymal and cavitary disease both upper lobes in 1959. Nodular disease both lower lobes. Required 50 units insulin daily. Faced with resection and thoracoplasty bilaterally in a severe diabetic, LUL bronchus ligated, but not divided, on Nov. 9, 1959. Discharged from hospital 11 days later. Fatal hemoptysis at home on Dec. 18, 1959. Autopsy not done. Question remains whether hemorrhage arose from LUL or from a contralateral cavity.

Comment: Failure. The bronchus should have been divided and a relaxing extraperiosteal thoracoplasty performed.

Fig. 22.

CASE 23.—(Fig. 23; J. B., 49, white male.) Diabetic, chronic alcoholic. All lobes involved in 1951. Cavities in RUL, LUL, and apex of LLL. In spite of triple chemotherapy, cavities enlarged, and, in 1958, a cavity appeared in apex of RLL. Organisms resistant. Pulmonary function markedly reduced. On Jan. 18, 1960, LUL bronchus and its individual segmental bronchi were doubly ligated and not divided. B-6 also ligated. Five-rib thoracoplasty done. Cavities closed 8 days later, only to re-open 2 weeks later. Fatal hemoptysis occurred on Feb. 10, 1960. Autopsy showed hemorrhage from cavity in opposite lung. The doubly ligated bronchi had sloughed, and loculated empyema was present.

Comment: Failure. The bronchi should have been divided to permit bronchial retraction away from the hilum, and medial cavity to collapse. Not necessary to remove ribs.

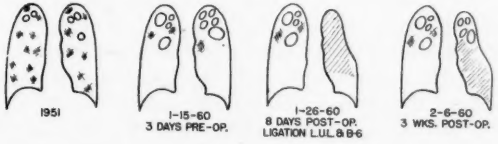

Fig. 23.

CASE 24.—(Fig. 24; A. N., 35, white male.) Onset 1957 in Puerto Rico. Presented in New York City early in 1958 with RUL cavity. Disease progressed and drug resistance developed after 2 years. Both upper lobes contracted. Trachea distorted. MBC, 29 L. per

minute. On April 22, 1960, RUL bronchus and B-6 divided. Periosteum elevated from ribs 1 to 4 posteriorly. Cavities closed. Too early for evaluation.

Comment: Operation tolerated well in spite of marked impairment of pulmonary function.

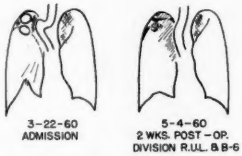

Fig. 24.

CASE 25.—(Fig. 25; F. T., 75, white male.) Known to have scarring and calcific foci in RUL for many years. First clinical evidence of tuberculous activity in 1957. Cavity RUL. Sputum positive. After 22 months chemotherapy, cavity closed and sputum converted. Cavity re-opened in October, 1959, sputum positive, organisms resistant. Advanced age and resistant organisms indicated bronchial division as procedure of choice. RUL bronchus divided and periosteum elevated from ribs 1 to 4 on April 26, 1960. Cavity closed. No sputum.

Comment: Successful case, 75-year-old patient. Effective circumferential cavity collapse.

Fig. 25.

TECHNICAL CONSIDERATIONS

The Incision.—A standard posterolateral thoracotomy incision is extended sufficiently high in the interscapular region to permit performance of an extraperiosteal thoracoplasty, if indicated. The pleural cavity is entered through the bed of the fifth rib, or through the fifth interspace if desired.

Lung Mobilization.—Cases of long-standing, cavitary lesions often present a severe form of obliterative pleuritis. Under these circumstances, exposure of the lobar bronchus can be difficult, since it is concealed by the inflated, adherent lung. The hilar structures may be approached in either of three different planes: the intrapleural plane, the extrapleural plane, and the extraperiosteal plane, which becomes extrapleural as one approaches the mediastinum. Mobilization of the lung in the intrapleural plane can damage the parenchyma and produce small, but undesirable, alveolar air leaks. Therefore, mobilization of the lung in the extrapleural or the extraperiosteal plane is preferable.

Lung mobilization is hazardous when the inflammatory reaction has been so violent as to obliterate the extrapleural space and fuse the diseased lung to the periosteum and to the intercostal muscles. This finding usually indicates that the cavity wall is immediately subpleural. A persistent effort to dissect in this plane may prove disastrous for two reasons. First, the underlying cavity may be inadvertently entered and, second, the nutritional blood supply to the cavity wall or underlying lung may be interrupted. This consideration is extremely important when it is recalled that the bronchial artery is to be divided along with the bronchus.

Lung mobilization in one plane or another is desirable because it allows the diseased parenchyma to collapse when the bronchus is divided. Adequate collapse will tend to ensure the obliteration of intersegmental communications and thereby permit atelectasis to occur, with its beneficial effects on healing. We believe that these pathways between segments or lobes, at the bronchiolar or alveolar levels, if not obliterated, may provide devious routes for acid-fast bacilli to reach the tracheobronchial tree and for collateral ventilation to occur, and thus prevent the desired collapse.

When lung mobilization and hilar exposure can be accomplished easily through the intrapleural or extrapleural plane, it is likely that lung collapse can occur, since it is not prevented from doing so by chest wall adhesions. However, if the bronchial ligation and division is to be segmental or if it is to be lobar in lungs having incomplete major fissures, we believe that a selective, extraperiosteal thoracoplasty over the cavity area will ensure lung collapse by obliterating these potential, retrograde channels. Since extreme therapeutic collapse is not required, the deformity of the standard thoracoplasty can be avoided by leaving the ribs in place. This concept of "circumferential collapse" is portrayed in Fig. 26. In addition, increased negativity of intrapleural pressure, because of the imposed atelectasis, is obviated by extraperiosteal thoracoplasty, thereby protecting areas of disease in the ipsilateral or contralateral lung against mediastinal shift and overdistention.

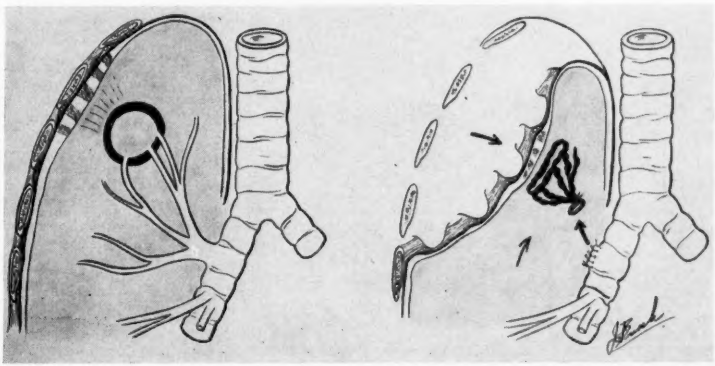

Fig. 26.—This drawing demonstrates the concept of "circumferential cavity collapse." *A*, The pleura adjacent to the cavity is adherent to the periosteum and intercostal muscles. Multiple segmental bronchi communicate with the cavity. *B*, Lung mobilization has been carried out in the extraperiosteal plane over the adherent zone to provide lateral cavity collapse, while preserving the chest wall collateral blood supply to the cavity. Recoil of the divided upper lobe bronchus provides, in addition to the lateral collapse, an accordion-like relaxation of the medial cavity wall.

The Hilar Dissection.—A well-padded Penrose drain is passed around the main bronchus. Traction on the main bronchus then permits easy and accurate identification of the desired bronchus or bronchi. The major bronchial arteries may be visualized, and branches to other lobes carefully preserved.

Division of Lobar Bronchi.—As soon as the proper bronchus has been identified and isolated, it may be divided. The proximal stump is closed with interrupted silk sutures and covered with viable tissue. The distal stump is doubly ligated with 1-0 silk, and allowed to recoil into the depths of the pulmonary parenchyma, enabling collapse of the medial wall of the cavity. It was reasoned that ligation of the distal stump was preferable to closure by interrupted sutures, since the latter might act as small wicks along which extravasation of cavity contents might occur (Fig. 27).

Division of Segmental Bronchi.—Segmental bronchi are divided at their origins between doubly ligated 1-0 silk ligatures placed 1.5 cm. apart (Figs. 28-29). Segmental bronchi in

the left upper lobe usually are concealed by several branches of the pulmonary artery. We have not seen adverse effects from ligating one or two of these vessels in approaching the underlying bronchus. Collateral ventilation must be dealt with when ligation and division are at the segmental level. Figs. 28 and 29 suggest methods of management in conjunction, ideally, with extraperiosteal "circumferential collapse," as shown in Fig. 26.

Pleural Drainage.—One intercostal tube is placed in the pleural cavity for purposes of suction drainage and re-expansion. If care has been exercised in mobilizing the lung and no significant air leaks are present at the time of closure, the tube can be removed the following day and the patient allowed out of bed.

RESULTS OF OPERATION

While it is customary to judge a surgical procedure on the basis of results obtained, the presentation of charts and graphs in this report would shed no light on the merits or faults of bronchial ligation and division as we envision it today. We believe that we have learned much about case selection, and have

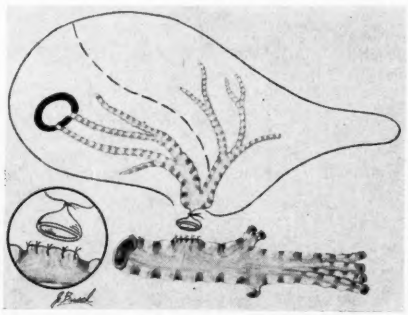

Fig. 27.—The operator's view of the posterior aspect of the right upper lobe, which is retracted anteriorly. The entire lobar bronchus has been divided, to prevent collateral ventilation from the uninvolved anterior segment. The details of proximal bronchial suture and distal bronchial ligation are shown.

developed concepts on the proper conduct of the operation, all at the expense of the 25 unusually diverse cases in this original report. The application of our present concepts to future cases will determine the worth of this operation.

Three patients were accepted for bronchial ligation and division as a "desperation measure" (Cases 3, 10, and 12). Each was considered an operation failure, although without operation an early fatal outcome was certain. Two died with bronchopleural fistula and empyema, while the third died with pulmonary insufficiency. The operation did not appear to alter his progressive deterioration.

Two other fatal results were Cases 22 and 23. Each of these had fatal pulmonary hemorrhages, 1 month and 3 weeks postoperatively. The former patient, in our present concept, should have had a relaxing extraperiosteal thoracoplasty, in addition to bronchial division. Her clinical course had been excellent up to the day of death. The site of hemorrhage could not be determined without autopsy. The other patient bled from a contralateral cavity, proved at autopsy.

Three additional deaths occurred from causes unrelated to the operation. Case 1 had cavity collapse and sputum conversion, but died after 6 weeks with amyloid uremia. Case 13 also had an excellent operative result, with cavity closure and sputum conversion, but died after 6 months with a pulmonary embolus following herniorrhaphy. Case 7 had successful bronchial ligation and division for pulmonary hemorrhage. He died with leukemia 6 months later.

Three patients still living were obvious operation failures. Case 9 required completion right pneumonectomy for middle and lower lobe bronchiectasis, persistent basilar cavity, and positive sputum. Previous to division of B-9 and

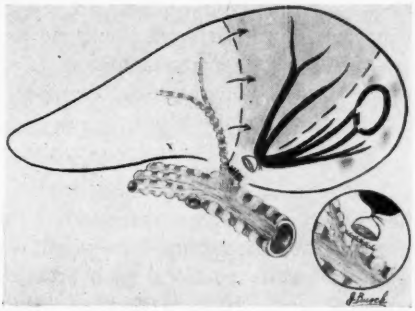

Fig. 28.—The operator's view of the posterior aspect of the left upper lobe, which is retracted anteriorly. The cavity is located in the apical-posterior segment. This bronchus and the adjacent anterior segmental bronchus have been divided. The lingular segments have been preserved. While collateral ventilation can occur into the anterior segment from the lingula, it was reasoned that collateral ventilation would not traverse this blocked segment (see Case 15).

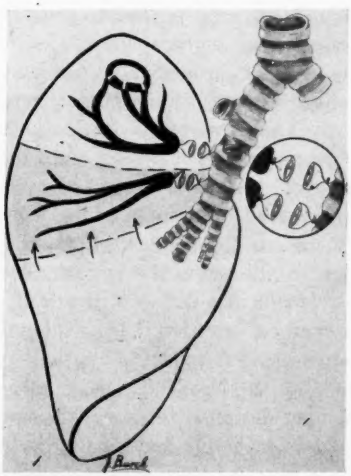

Fig. 29.—The right lower lobe is shown with a cavity in the superior segment. (The upper and middle lobes have been removed for clarity.) The superior segmental bronchus and an accessory sub-superior bronchus have been ligated and divided. The fortuitous presence of the latter provides an interposed segment which can aerate only collaterally from the basilar segments. Case 2 presented this situation in the left lower lobe.

B-10 the patient had had a right upper lobectomy. In retrospect, bronchial division performed in the remaining markedly overdistended lung without relaxing thoracoplasty was doomed to failure. Case 11 has persistent cavities and positive sputum, both of which might have been averted had an extraperiosteal thoracoplasty been combined with the bronchial division procedure. Case 21 developed bronchopleural fistula and empyema as the result of an ill-conceived attempt to preserve the anterior segment of the right upper lobe by creation of an artificial intersegmental fissure. Each of these failures is avoidable according to present concepts.

The remaining 14 patients, in addition to the 3 who died from unrelated causes, had excellent results, with cavity closure and sputum conversion.

In summary, bacteriologic negativity and cavity closure were accomplished in 17 cases, and 1 patient was negative preoperatively (Case 7). Of the 6 patients not converted, 3 are dead, 1 is negative following pneumonectomy, and 2 remain under treatment for their complications.

DISCUSSION

Acceptance of the concept of operative occlusion of the bronchus is facilitated when it is realized that auto-occlusion occurs in the natural course of cavitary tuberculosis. In 1940 we observed a left main bronchus that was pinpoint in size, and pus aspirated from it contained acid-fast bacilli. Five later bronchoscopic examinations failed to disclose an opening to the left main bronchus, and sputum cultures became negative. Chest films showed opacification of the left hemithorax. Auto-occlusion of a main bronchus had occurred.

An example of auto-lobar occlusion was provided in 1940 by a patient with a loud wheeze, positive sputum, and a pinpoint opening to the left upper lobe bronchus beneath an unsuccessful thoracoplasty. Stimulated by the work of Adams and Vorwald, the stenosed bronchial orifice was treated on three occasions with 35 per cent silver nitrate. Each time the wheeze disappeared and the sputum became negative, only to return 10 days later as the bronchus reopened. Eventually the bronchus closed permanently and, now, 20 years later, the wheeze is gone, the sputum is negative, and no cavity can be demonstrated. A similar lobar occlusion occurred in Case 2 of this report.

Auto-occlusion of a segmental bronchus was observed in a 49-year-old male who presented with infiltrative disease in the apical-posterior segment of the left upper lobe and with positive sputum. After 1 month of isoniazid and PAS, the sputum converted and remained negative. The residual disease focus was resected 8 months later and revealed fibrous closure of the segmental bronchus.

Ligation and division of the bronchus, as a surgical solution to cavity closure, is a technical adjunct designed to mimic the natural course of the disease. The procedure is old in principle, but its therapeutic realization was surprisingly slow to occur. To realize that auto-occlusion of the bronchus sometimes occurs in the natural course of cavitary disease was not enough. It was essential to learn that obstruction to drainage by bronchial occlusion was not harmful. We had to be assured that no secondary organisms were trapped in

the cavity to set the stage for a fulminating lung abscess. Circulatory shunts, nutritional hazards with cavity rupture, bacteremia, and other potential hazards proved to be either nonexistent or avoidable surgically. Our errors were original errors, since we had no recourse to the mistakes of others.

The majority of authors reporting on the various aspects of collapse therapy focused their attentions on the technical maneuvers by which they achieved successful results. For example, the proponent of pneumothorax might emphasize the size and frequency of refills; in extrapleural pneumothorax it was the degree of pressure; or if the surgeon had designed an improved type of thoracoplasty, he described in detail its technical merits. It is remarkable in retrospect how little attention was paid to the role of bronchial occlusion in the ultimate success of these varied collapse procedures. But now, we believe that surgical division of the bronchus should be recognized as a distinct surgical entity, not concealed beneath the therapeutic guise of thoracoplasty, pneumothorax, or other type of treatment, but to occupy its own definite place in the surgical treatment of cavitary tuberculosis.

This relatively new procedure, surgical division of the bronchus, is not to be compared with or substituted for pulmonary resection in the treatment of cavitary tuberculosis. In general, ligation and division of the bronchus begins where resection leaves off. That is to say, when the indications for resection have to be extended precariously, then bronchial division may prove to be a more acceptable solution.

In reviewing 300 cases of segmental resection,[63] it was noted that bronchial fistulas were most likely to occur when the upper lobe and the superior segment of the lower lobe were resected simultaneously. The fistulas were thought to be due to the difficulty in obliterating the residual pleural space. This observation was especially true on the left, when the lingula was resected along with the rest of the upper lobe. In such instances, to avoid a bronchopleural fistula, a preliminary thoracoplasty might be done so as to eliminate a space problem at the second stage when the resection is accomplished. In some cases the surgeon may elect to perform the thoracoplasty at the time of the resection, but the dimensions of such a combined operation are to be respected. Ligation and division of the proper bronchi, under these circumstances, offers an alternate solution for patients in whom the indications for resection are being extended beyond reasonable risk.

In an extensive report from England[64] on the surgical management of tuberculosis, it was concluded that there still is a significant place for the classical therapeutic thoracoplasty, if the hazards of extensive and complicated resections are to be avoided. This philosophy has great merit, but to it might be added that if the effectiveness of the thoracoplasty is to be ensured, then the procedure should be supplemented by the surgical division of the proper bronchi. The classical therapeutic thoracoplasty requires not only that long segments of ribs be removed, but that they must be removed in sufficient number to get well below the disease for an effective collapse. Such a procedure is deforming, it must be done in two or three stages, and it is costly to pulmonary function. The

selective extraperiosteal thoracoplasty which is proposed at the time of bronchial division is not deforming, it can be done in one stage, and only short segments of ribs are stripped of their periosteum posteriorly. Therefore, function in the anterior chest is carefully preserved.

SUMMARY

1. Atelectasis exerts a favorable influence on pulmonary tuberculosis.

2. The key to successful cavity collapse is permanent occlusion of the draining bronchus or bronchi.

3. Auto-occlusion of the bronchus is an inconstant but fortunate event in the natural course of tuberculosis, and is in no way disturbing to the general physiology.

4. Ligation and division of the draining bronchus can mimic the beneficial effects of auto-occlusion and accomplish cavity closure and bacteriologic negativity.

5. A concept has been presented for the safe conduct of this operation, developed from experiences with 25 clinical cases.

6. Low morbidity and mortality rates will be accomplished if these basic concepts are followed.

7. Many patients unsuitable for resection or major collapse measures can be treated successfully by bronchial ligation and division.

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DISCUSSION

DR. KENJI KAWAMURA, Kyoto, Japan.—Thanks for the privilege of the floor, Dr. Adams—also thanks to Dr. Chamberlain for the report of such fine results in the cases of ligation of the bronchus.

My comrade and my associate, Professor Kitagawa, also had 3 cases of bronchus ligation for tuberculous cavities 5 years ago, which were reported in Japan, but the results were not so good. Dr. Chamberlain's cases are all very good. It comes, perhaps, from nice selection of the locale of the ligation of the bronchus, I think.

Now I should like to speak about another operation for the same advanced, poor risk case of tuberculosis; that is, extrafacial bone chips packed with coagulated blood. I have used the rib transplantation on the pleura in 12 cases at first, and made sure of their healing process during 3 to 7 years after surgery. According to these observations, the operation was improved by the use of bone chips filled with coagulated blood. The effect of bone transplantation in the tissue near the tuberculous lung is based on experimental results which show calcium precipitation in tuberculous foci from bone calcium, and also from tooth. (Slide) This shows bone chips that were taken from a resected rib.

(Slide) Next you see bone chips mixed with homologous blood coagula; (slide) and then you see the operation, putting them into the extrapleural space after pulmonary collapse.

(Slide) This is a roentgenogram before operation of one of the cases (slide), and the next is 2 weeks after (slide), and then the next is after 3 months.

We have had 7 patients with such operations for advanced tuberculosis, and until now all of them have had good results. The longest case is 3 years, and the shortest case is one half a year.

DR. JOSEPH J. TIMMES, St. Albans, N. Y.—We have also had experience with division of the bronchus in the surgical treatment of cavitary tuberculosis in the past year and a half, and our results thus far parallel those of Dr. Chamberlain. In the recent past we have sectioned the right main-stem bronchus.

(Slide) This first slide represents a woman, 40 years of age, who has had many years of treatment for tuberculosis starting with a pneumothorax, and many attempts at medical therapy using various combinations of drugs. She came to us with a destroyed right lung, positive sputum, and the organisms resistant to the drugs. Her maximum breathing capacity was 24 liters per minute preoperatively.

We divided the bronchus and then closed each end with interrupted sutures, not using the ligation technique of Dr. Chamberlain. At the conclusion of the operation we did a tracheostomy, kept her on assisted ventilation for 48 hours, and her postoperative course was uncomplicated.

(Slide) Arterial studies done 2 months postoperatively show there is now no desaturation at rest, or after exercise. With 100 per cent oxygen the saturation increased to 100 per cent.

We can interpret these studies as indicating that the shunt which must be present, since the pulmonary artery and the veins are left intact, must be minimal, and I wonder if Dr. Chamberlain would comment about this phenomenon.

DR. WILLIAM M. TUTTLE, Detroit, Mich.—I am going to discuss this paper because I happened to be there when dogs' bronchi were being cauterized, and that goes back approximately 30 years.

Now, I do not believe that this is the right surgical approach to this problem. It did not work in the few clinical cases which I hope Dr. Adams will tell you about, although it did work in dogs. In 1 case shown here today I would have taken the lung out. In other words, more maneuvers are used to tie a bronchus or cut a bronchus and sew it on both sides than we use to take the lobe out. This, to me—I must speak frankly—is against all surgical principles. The principle of disease therapy is to cure the disease by medicine or by God or by surgery, [laughter] and I just can't go along with this. You leave the disease in and let the patient live with it, or you take it out, or you cure it by various medicaments.

DR. LAWRENCE M. SHEFTS, San Antonio, Texas.—I know that many in the audience have tried the very thing that Dr. Chamberlain has very ably presented here today, but I'd like to make one point: Dr. Chamberlain has not stopped doing resections, and neither will most surgeons here. This operation is fraught with dangers, and I think it should be left in the hands of the few who still want to continue with it until there is a larger series of cases to place it on a broader basis. But today there are very few patients to whom we cannot offer resectional surgery with a very respectable mortality and morbidity.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—The previous discussers have not, in my opinion, noticed that the type of material Dr. Chamberlain has presented is the type of material in which resection therapy would not be possible to carry through. There is a group of cases which are drug resistant, bilateral, and in which there is so much disease spread to other parts of the lungs that if resection were tried the patients would end up with empyemas and bronchial fistulas in practically every case. I think that in this limited small group, Dr. Chamberlain's suggestion is both sound and a very good one.

PRESIDENT ADAMS.—Since reference was made to our earlier work, I will merely make two remarks.

One is that the tubercle bacillus which we used would always lead to the death of the dogs, and it was very striking how relatively little or no tuberculosis developed in atelectatic lungs.

The second point is that the clinical cases selected—and there were only 4—all had huge cavities with secondary infection, and we were unable to occlude completely the bronchus in these cases.

When Dr. Chamberlain first spoke to me about his experience with obstruction of the bronchus by division and suture, I had the feeling that the results of obstruction should be similar in patients to those seen in animals. I would be very inclined to agree with Dr. Crafoord that the risk of resection would be very great in those cases in which the organisms were resistant to the drugs and the involvement was as great as he showed.

DR. CHAMBERLAIN (Closing).—I would like to thank all the discussers, especially Dr. Crafoord, and to point out to you the one point that Dr. Timmes did not make. I happen to know about his case. The patient technically was hopelessly nonresectable. It was impossible to remove the lung as it was described to me, and I am sure that his solution was the proper one.

Dr. Shefts made some excellent points. He pointed out that there are definite dangers to the ligation and division of the bronchus, and in the manuscript we have gone into great detail to point out the dangers.

I would like to close by adding a word of caution. I hope that you will not return to your respective environments and attack every therapeutic failure by ligating and dividing the bronchus. We have made many errors, and I hope that before you proceed with this operation you will take advantage of these mistakes by following certain basic principles of case selection and operative technique which we have formulated.

THE CULTURE OF TUBERCLE BACILLI FROM RESECTED SPECIMENS OF "NEGATIVE" PATIENTS

George J. Willauer, M.D., Charles Fineberg, M.D. (by invitation), Robert G. Johnson, M.D. (by invitation), and William P. Coghlan, M.D. (by invitation), Philadelphia, Pa.*

THE CLASSIC PAPER entitled "Simple Excision in the Treatment of Pulmonary Tuberculosis" by Ryan, Medlar, and Welles[1] was read by Dr. Ryan before the Thirty-first Annual meeting of this Association in Atlantic City in April of 1951. Since that presentation there has been a fundamental change in regard to the complete treatment of pulmonary tuberculosis. The principles of treatment no longer concern themselves with arrest but rather with excision of the residuals of the disease and possible bacteriologic cure.

A major area of disagreement about the indication for pulmonary resection in tuberculosis concerns itself with patients who have residual disease and negative sputum. Should these patients be subjected to resection or be continued on bed rest and antimicrobial therapy? D'Esopo and his associates[2] have stated that the relapse rate is no different in resected and unresected nodular residuals. Culture of resected specimens by this group revealed that most of the organisms were nonviable. Hobby and co-workers,[3] with special culture techniques, have demonstrated that tubercle bacilli present in closed necrotic lesions after long-term chemotherapy are not as "dead" as has been suggested by others.

Although investigators have identified tubercle bacilli in resected caseous nodules and cavities of patients with negative sputa, these organisms have been difficult to culture[4-9] (Table I). The reported incidence of live bacilli

TABLE I. PREVIOUS SERIES: SPUTUM-NEGATIVE PATIENTS

YEAR	INVESTIGATORS	NO. OF PATIENTS	TOTAL POSITIVE RESECTED SPECIMENS
1952	D'Esopo et al.[4]	84	15%
1955	Hobby et al.[5]	43	72%
1955	Adler et al.[6]	103	18%
1956	Stewart et al.[7]	47	23%
1956	Bell[8]	147	40%
1956	Wayne and Salkin[9]	201	15%
1957	Hurford and Valentine[10]	50	38%
1959	Nat. Jewish Hosp.[11]	113	5%
1960	Willauer	29	85%

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has varied from 5 to 72 per cent. Auerbach[12] has pointed out the danger of supposed negative lesions discharging viable tubercle bacilli into the tracheobronchial tree.

It was the purpose of this study to investigate the incidence of viable organisms in resected specimens from a series of patients with negative sputa.

Many investigators[13] have used elaborate techniques for the culture of tubercle bacilli from resected lung tissue. Some groups have kept the specimens at 4° C. for indefinite periods of time before taking material for culture. Others have used homogenizing procedures and digestion of material with sodium hydroxide or sulfuric acid. Hobby and her group washed the homogenate in bovine albumin in order to eradicate the "toxic" components of necrotic debris.

In contrast to these methods, we have utilized a simple and direct approach. Immediately following the surgical procedure, the surgeon examined the resected specimen utilizing sterile precautions. Areas of cavitation and nodularity were incised and the caseous material was transferred with a sterile loop directly to a culture tube slant. A heavy inoculum was used and the entire surface of the slant was streaked. The formula of the egg yolk medium which was used is given in Table II. The streaked slants were incubated at 37° C. They were read at weekly intervals and discarded at the end of 8 weeks.

TABLE II. EGG YOLK MEDIA

Fresh egg yolk	100 ml.
Distilled water	33 ml.
Sterile glycerine	3.2 ml.
2% sterile malachite green	1.3 ml.
Inspissated for one hour at 84° C.	

This study extended over a period of 6 years, 1952 to 1958. During this time 125 patients have had pulmonary resections. There were 89 lobectomies, 17 wedge resections, 11 segmentectomies, and 8 pneumonectomies. The patients were both private and ward. Because several physicians handled the medical care of these patients, their antimicrobial therapy was varied. The surgical

TABLE IIIA. BACTERIOLOGY OF PREOPERATIVE SPUTA AND RESECTED SPECIMENS

PATIENTS	SPUTUM	RESECTED SPECIMEN
91	+	+
25	−	+
5	+	−
4	−	−
125		

TABLE IIIB. DURATION OF NEGATIVE SPUTUM

MONTHS	NO. OF PATIENTS
0 to less than 3	9
3 to less than 6	3
6 to less than 9	10
9 to 12	3
	25

management was directed by one of us (G. J. W.). Of the 125 patients who were operated upon, 29 had negative sputa for periods of 1 to 12 months prior to resection (Table IIIA, IIIB). Twenty-five of the 29 patients with negative sputa proved to have viable tubercle bacilli in their resected specimens and form the basis of this report. The surgery performed on these patients consisted of 3 pneumonectomies, 10 lobectomies, 8 segmentectomies, and 4 wedge resections. The type of lesion found in relation to the surgical procedure performed is listed in Table IV. The involvement found at operation necessitating pneumonectomy in 3 patients cannot be regarded as residual disease. These 3 cases are included because the preoperative sputum was negative and the resected specimens grew tubercle bacilli.

TABLE IV. CORRELATION OF SURGERY AND PATHOLOGY

SURGICAL PROCEDURE	NO.	CAVITARY	NODULAR
Pneumonectomy	3	1	2
Lobectomy	10	8	2
Segmental resection	8	2	6
Wedge resection	4	1	3
Totals	25	12	13

Four patients had negative sputa prior to operation and culture of the resected specimens was negative. The remainder of the group, 96, had positive sputa at the time of resection. Resected lung tissue from 5 of these patients failed to grow tubercle bacilli.

The preoperative antimicrobial therapy was either continuous or interrupted. Included under continuous therapy were those patients who had pulmonary tuberculosis diagnosed on admission and who received continuous antimicrobial therapy to the time of resection. All others were classified as interrupted. In the 25 patients we are discussing, 15 had received continuous therapy and 10 had interrupted therapy. The shortest duration of continuous antimicrobial therapy was 4 months and the longest 27 months. The average was 11 months. These patients all received various combinations of streptomycin, isoniazid, and para-aminosalicylic acid. Fifteen patients were on two drugs; 10 patients were on three drug therapy. The majority of those on two drug therapy received streptomycin as one of the drugs.

Follow-up data were obtained on every patient in this group (Table V). This information was obtained from either the records of the Eagleville Dispensary or from the patient's physician. All patients in this series were discharged on antimicrobial therapy. The type and duration of antimicrobial therapy was thereafter controlled by the patient's physician. One patient died of pulmonary insufficiency following resection on the opposite side 1 year after the original operation. The only true failure of the group was in an uncooperative patient who showed evidence of activation in the lower lobe on the side of the resected lung and positive sputum 5 years following operation. The remaining 23 patients are well, sputa negative, and only 2 are still on antimicrobial therapy.

TABLE V. POSTRESECTIONAL FOLLOW-UP

NO. OF PATIENTS	YEARS AFTER RESECTION	SPUTUM	ANTIMICROBIAL THERAPY	RESULTS
1	8	–	No	Well
7	7	–	1	Well
4	6	1 +	1	3 well
		3 –		1 spread of disease
1	5	–	No	Well
7	4	–	No	Well
2	3	–	No	Well
2	2	–	1	Well
1	1	1 +	1	Died 1 year later of pulmonary insufficiency
Total 25				

The very high percentage of viable tubercle bacilli obtained from resected specimens in this series is in contrast to other reported series. We believe that two important factors have led to this result: (1) the transfer of material was done immediately by the operating surgeon from the freshly resected lung tissue, and (2) the material was neither traumatized by maceration or by freezing techniques.

SUMMARY

1. In a series of 125 consecutive patients with pulmonary tuberculosis who had pulmonary resections, 29 had had negative sputa for a period of 1 to 12 months prior to resection.

2. Positive cultures for tubercle bacilli were obtained from the resected lung tissue in 25 of these 29 patients.

3. There were no operative deaths. One patient died a year later following a subsequent resection on the opposite side.

4. The patients have been followed from 1 to 8 years postoperatively. Twenty-three are clinically well. In all cases the sputa have remained negative.

CONCLUSIONS

1. Patients with negative sputum and residual lesions have viable tubercle bacilli in the resected specimens in a high percentage of cases.

2. Resectional surgery in this type of patient affords a better chance for permanent cure.

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DISCUSSION

DR. PAUL C. SAMSON, Lafayette, Calif.—With the advent of chemotherapy there has developed a new classification in tuberculosis, the so-called "open-negative," and I would like to confine my remarks to the open-negative group rather than to the broader series of cases which were so ably presented by Dr. Coghlan.

The reason that I think it is important to keep hammering at this is that our medical confreres are feeling their oats a little these days, and a good many of them feel that if they once can get the sputum negative, that that is the answer to the problem, and we perhaps see less of these patients referred for surgery now than we did even a few years ago.

Therefore, I think it's important to keep emphasizing the fact that with proper laboratory facilities and careful techniques, as you have just heard, many of these patients can be proved to contain viable bacilli, and, therefore, in my opinion, resection should be done.

Dr. Shebart and I reviewed a series of cases recently from the VAH Livermore. Our figures are similar to Dr. Coghlan's over a 2-year period. Thirty-three cases in a group of 122 consecutive resections satisfied the requirement of "open-negative," which means a cavity presumed or ascertained to be present from the x-ray, and sputum negative for at least 3 months.

Of these 33, 23 (70 per cent) yielded positive cultures of the resected specimen.

Now, it's interesting that several of the cultures of resected specimens were negative at the end of the 3 months. Three patients whose cultures of the resected specimens were positive had been negative to all clinical means for 12 months prior to surgery.

I think this paper is important because of some change in attitude on the part of our medical colleagues. Particularly in patients in the open-negative group I believe resection should almost always be done.

DR. DAVID V. PECORA, Ray Brook, N. Y.—I think when we speak of the open negative group we should define our terms. I do not believe that it represents a homogeneous group. This group discussed today is certainly not homogeneous, because it has included patients who had interrupted therapy, and also therapy of varying duration.

If we define the therapy carefully and also the duration, then we can obtain a somewhat different result.

We have not encountered a high relapse rate in patients treated with various combinations of streptomycin, PAS, and INH compounds, providing the organisms are susceptible and the therapy is continuous and prolonged. Although we attempt to remove cavitary disease whenever possible, we have not encountered a high relapse rate in those patients who, for one reason or another, have not had surgery, provided INH is one of the drugs employed.

Since January, 1950, we have made bacteriologic studies of 303 lesions resected from patients receiving various combinations of streptomycin, PAS, and INH continuously over prolonged periods. Our methods of culturing the organisms are similar to those presented.

Concentrated smears were positive for acid-fast bacilli in 66 per cent of the patients who had been sputum negative by culture for 6 months or less prior to surgery, and 64 per cent of those who had negative sputum for more than 6 months prior to surgery. On the other hand, cultures of resected pulmonary tissue were positive for tubercle bacilli in 9 per cent of the patients who had negative sputum cultures for 7 months or less prior to surgery. In no instance did we find a positive culture of tissue in a patient who had negative sputum cultures for over 7 months prior to surgery.

We have found no correlation between the incidence of postoperative tuberculosis complications or reactivations and the presence of nonculturable tubercle bacilli in the tissues. We have had no early tuberculous complications and less than 2 per cent late tuberculous complications in patients who have not harbored culturable tubercle bacilli in the resected tissues.

DR. LAWRENCE M. SHEFTS, San Antonio, Texas.—Very briefly, I agree emphatically with Dr. Coghlan's conclusions. In 20 to 25 per cent of our resected specimens in patients who have had a negative sputum for long periods of time, we were able to obtain organisms from the cavities. They are in the wall, thick and hard though it may be.

Many papers are being presented in today's literature on the follow-up of open negative cavities. When the internist figures a relapse rate of 5 per cent, and says that our relapse rate is the same from surgery, what is the point of operating? The point is that it is a difference in terminology between open negative cavities and open healed cavities.

COLON REPLACEMENT OF THE ESOPHAGUS IN CHILDREN FOR CONGENITAL AND ACQUIRED DISEASE

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Cleveland, Ohio

INTRODUCTION

In previous reports,[9, 11] we have presented our observations in patients operated upon for benign and malignant disease, in which segments of the colon have been used to reconstruct all or part of the esophagus and stomach. Among these the most gratifying results have been obtained in children with congenital esophageal defects and corrosive destruction.[2, 3, 5, 8] Heretofore, in these patients, the most successful reconstructions of an adequate swallowing mechanism have employed anterior, subcutaneous or retrosternal jejunal transplants.[4, 6, 7, 14]

The purpose of this paper is to present our operative technique and observations in children upon whom we have reconstructed the esophagus with the colon.

OPERATIVE TECHNIQUE

The operation is performed in one or two stages, depending upon the nature and extent of the disease.

Preoperative preparation consists of restoration of nutritional and chemical balance and sterilization of the colon. The latter is prepared for 2 to 4 days with neomycin (1 gram) every 6 hr. by mouth or through the gastrostomy tube, if this had been inserted for feeding purposes.

If the entire esophagus is to be reconstructed, the baby is operated upon in the supine position. If the child has had a previous esophagostomy, this is dissected from the surrounding tissue. The esophagus is exposed in the neck through an incision along the anterior border of the right sternocleidomastoid muscle (Fig. 1). The strap muscles are divided transversely over the thyroid gland. The esophagus is isolated posterior to the trachea just above the manubrium and dissected upward. The recurrent laryngeal nerve is identified and preserved.

Two operating teams have been employed. The abdomen is opened through a long upper midline incision from the xiphoid to below the umbilicus. The

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entire right colon is mobilized from the cecum to the hepatic flexure by incising its lateral avascular peritoneal attachments. The lesser peritoneal cavity is entered midway along the greater curvature and the gastrocolic omentum divided to the hepatic and splenic flexures. Thus, the entire colon is mobilized from the cecum to the splenic flexure. The ileocolic, right, and middle colic vessels are identified. To test the ability of the middle colic artery and vein to supplant the circulation of the colon, the right colic artery and vein are temporarily occluded with a bulldog clamp. In the interim the appendix and greater omentum are removed. If the circulation appears to be adequate, the right colic vessels are divided close to their origin. The proximal end of the bowel is transected at the ileocecal valve and the opening in the cecum is closed.

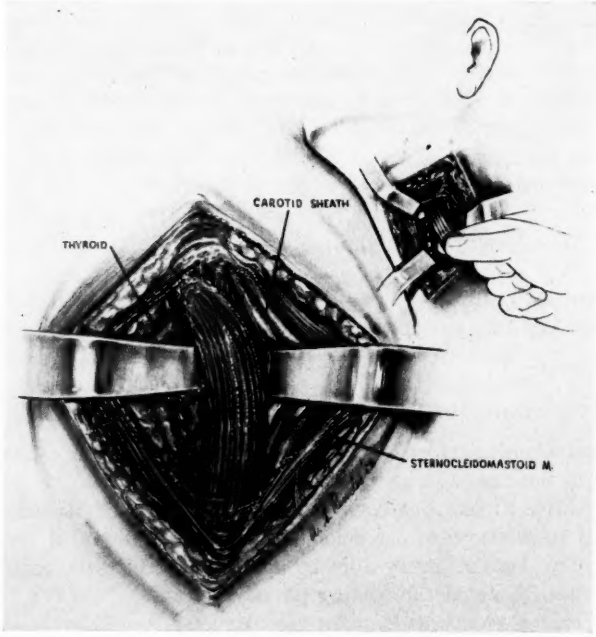

Fig. 1.—Exposure of the esophagus in the neck.

The right half of the colon is placed on the chest wall to determine its adequacy for esophageal reconstruction. If necessary, additional length can be obtained by further division of the mesentery on the right down to the origin of the vascular pedicle. A tunnel is created in the anterior mediastinum just posterior to the periosteum of the sternum from the xiphoid process to the manubrium by blunt dissection from below and above. The proximal end of the colon is passed into the neck, either in front of or behind the stomach, through this tunnel. The latter seems preferable because it offers additional length, and the duodenum is not compressed by the vascular pedicle. To widen the thoracic inlet it may be necessary to remove a V-shaped segment from the upper

sternum. Having determined that the cecum will reach the neck without compromising its blood supply, the colon segment is isolated by dividing the transverse colon. Thus, the entire segment is suspended upon a vascular pedicle comprised of only the middle colic artery and vein (Fig. 2). The cervical esophageal colon anastomosis is performed, end-to-end, with two or three layers of interrupted fine silk. If the distal esophagus is not resected at this time, a catheter is inserted into this section and brought out through a stab wound to create a mucus fistula. Simultaneously, an opening is made on the anterior wall of the stomach and the distal end of the colon is anastomosed to this organ. Either a pyloromyotomy or a pyloroplasty may be performed. A tube gastrostomy, if not already present for preoperative feeding, is created to de-

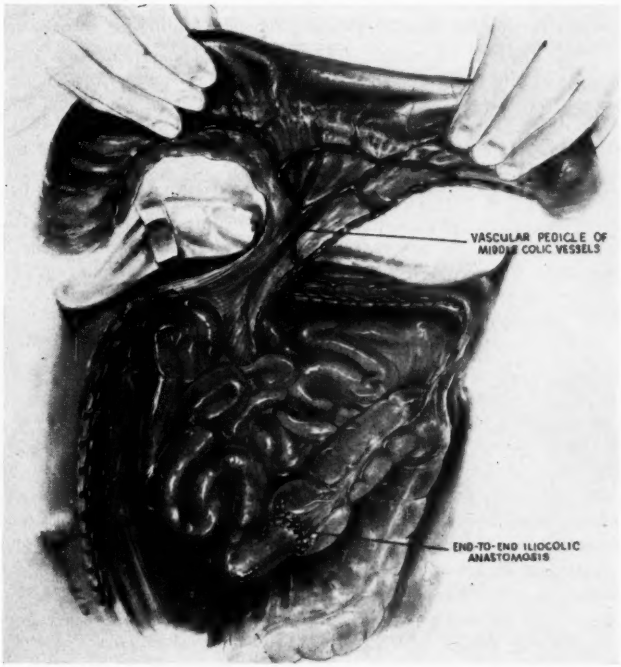

Fig. 2.—Isolated colon segment suspended on a vascular pedicle of the middle colic artery and vein.

compress the stomach in the early postoperative period. It may then be used for subsequent feedings until such time as the patient is able to eat normally. This maneuver obviates the necessity for an indwelling nasogastric tube. The continuity of the lower gastrointestinal tract is established with an end-to-end iliocolostomy.

Lesions within the thorax above the aortic arch are approached through a right thoracotomy and upper midline incision. The colon segment is delivered into the chest through an opening in the diaphragm anterior to the liver and placed along the anterior aspect of the right hilum.

Intrathoracic esophageal lesions below the aortic arch are approached through separate left abdominal and thoracic incisions. The diaphragm is transected from the hiatus outward. In this situation it is not necessary to mobilize the right colon. The transverse colon is usually of sufficient length to substitute for the resected esophagus. Following resection of the lesion, the proximal end of the bowel is passed into the left chest. The isoperistaltic esophagocolon anastomosis of the resected esophagus and the entire area are repleuralized. The opening in the cardia is closed and the distal end of the colon is anastomosed to the stomach anteriorly. A colocolostomy, pyloroplasty, and tube gastrostomy complete the operative procedure.

CASE REPORTS

CASE 1.—*Stricture of the lower esophagus following ingestion of corrosives.*

J. S., a 6-year-old boy, was admitted to University Hospitals on Oct. 19, 1953, shortly after swallowing muriatic acid. An emergency tracheotomy was performed because of difficulty in breathing. He was placed on cortisone and antibiotics. A barium swallow 1 week after admission demonstrated a stricture at the lower end of the esophagus and pyloric obstruction. Bougienage of the esophagus was successfully carried out but the pyloric obstruction persisted. Resection of the distal end of the stomach was performed on Dec. 10, 1953, a Billroth I type of procedure being performed. Despite repeated esophageal dilatations, dysphagia and vomiting persisted. Neuropsychiatric therapy was instituted because of absence of roentgenographic evidence of pyloric obstruction. Narrowing of the distal end of the esophagus was repeatedly evident by x-ray study and esophagoscopy. On several occasions it was necessary to remove a bolus of food from the esophagus. In June, 1955, x-ray studies of the esophagus and stomach showed 90 per cent gastric retention at the end of 6 hours. He was admitted to St. Alexis Hospital where revision of the gastroduodenostomy was done on July 1, 1955. The lower end of the esophagus was definitely narrowed, but there appeared to be normal passage of barium through this area. Following this, he was relieved of his symptoms only temporarily. On July 7, 1956, he was admitted to Cleveland Metropolitan General Hospital* for resection of the esophagus. Roentgenograms showed a persistent narrowing of the lower end of the esophagus with an adequate gastroduodenal stoma. On July 12, 1956, the lower end of the esophagus was resected and the transverse colon interpolated in an isoperistaltic manner between the esophagus and the stomach. His postoperative course was relatively uneventful. Tube feedings were begun on the seventh postoperative day and oral feedings on the tenth day. He was discharged on the sixteenth postoperative day at which time he was eating a normal diet. The gastrostomy tube was removed just prior to his leaving the hospital. Since then he has been completely asymptomatic. X-ray studies 1 year later at the Cleveland Clinic were normal. At the present time he can eat everything without discomfort or diarrhea. He weighs 58 pounds and is 56 inches tall.

CASE 2.—*Stricture of lower esophagus.*

R. M., a 5-year-old boy, was admitted to the hospital on June 20, 1957, complaining of difficulty in swallowing. His mother stated that he had swallowed lye 2 years previously. The subsequent stricture had been treated with frequent bougienage in another city. This was his first episode since the family had moved to Cleveland. X-ray studies of the esophagus showed narrowing at the lower end. On esophagoscopy, the scope could not be passed through the strictured segment. Dilatation was unsuccessfully attempted. He was operated upon on June 26, 1957. The left thorax was opened through the eighth interspace. The diaphragm

*Formerly Cleveland City Hospital.

was incised from the hiatus to the costal margin. The lower end of the esophagus was resected from the level of the inferior pulmonary vein down to the stomach. The distal transverse colon was easily delivered into the chest after dividing the gastrocolic omentum and freeing the splenic flexure. The colon was divided proximally and distally and a pie-shaped segment with its attendant blood supply was interpolated between the cut end of the esophagus and the stomach. The colon was reunited and a gastrostomy completed the procedure. His postoperative convalescence was uneventful. The gastrostomy tube was removed before his discharge on the twenty-second postoperative day.

Postoperative symptoms of abdominal cramps and diarrhea occurred but disappeared within 8 weeks. Since that time he has been entirely asymptomatic.

CASE 3.—*Delayed reconstruction of esophagus in tracheoesophageal fistula with atresia.*

Baby F was operated upon July 22, 1954, at the age of 4 days, for a tracheoesophageal fistula with atresia. After ligation of the fistula, the lower end of the esophagus was resected. A feeding gastrostomy and cervical esophagostomy were performed.

On Aug. 22, 1955, an anterior mediastinal colon transplant was performed. With the baby in the supine position, the abdomen was opened through a long upper midline abdominal incision. The colon was mobilized from the cecum to the splenic flexure. It was transected proximally and distally after the existence of length adequate for esophageal reconstruction had been determined. The cervical esophagostomy was dissected free and a tunnel created in the anterior mediastinum just posterior to the periosteum of the sternum. The proximal end of the colon segment which was suspended on a pedicle of the middle colic artery and vein was passed through the mediastinal tunnel into the neck. An esophagocolostomy and cologastrostomy were performed concomitantly. A colocolostomy reunited the lower bowel.

His postoperative course was uneventful except for the development of a cervical fistula. This healed readily and he was eating normally at the time of his discharge. On Dec. 15, 1955, he was admitted to the hospital because of difficulty in swallowing. It was obvious that there was a stricture at the esophagocolostomy but, because of severe diarrhea and an elevated temperature, a revision of the anastomosis was postponed. On December 18, the infant suddenly became cyanotic and dyspneic which necessitated an emergency exploration of the neck. The dilated esophagus which was adherent to the skin was entered first. The colon was markedly narrowed at the thoracic inlet. The stricture was manually dilated with a clamp until an adequate opening was obtained. The esophagus was closed and a tracheostomy performed. The convalescence was uneventful.

In June of 1957, another episode of complete obstruction occurred. A bolus of food was removed from the cervical esophagus and the stricture again dilated. Subsequently, on 3 separate occasions, bougienage of the narrowed segment has been performed. In the past year and one half this has not been necessary. At the moment, the child eats everything without experiencing dysphagia. He is 46 inches in height and weighs 45 pounds.

CASE 4.—*Stricture of the entire esophagus.*

B. S., a 30-month-old Negro male child, was admitted to Cleveland Metropolitan General Hospital on Nov. 20, 1956, because of persistent regurgitation of 2 weeks' duration. No history of ingestion of corrosive material could be obtained from the mother. Barium swallow on Nov. 23, 1956, revealed two areas of narrowing of the esophagus, one at the midportion and the other 2 cm. proximal to the cardia. Esophagoscopy on Nov. 27, 1956, demonstrated narrowing of the lumen at 3 cm. The mucosa appeared reddened and friable. No attempt was made to pass the esophagoscope beyond this level, but a biopsy was obtained which subsequently proved to be chronic inflammatory tissue. Several hours following this procedure, the baby developed crepitation of the neck. A roentgenogram of the chest revealed subcutaneous emphysema and a pneumomediastinum. A superior mediastinotomy and a tube feeding gastrostomy was performed immediately. His recovery was uneventful except for aspiration on 120 c.c. of straw-colored fluid from the left hemithorax.

Progress x-ray studies showed persistent narrowing of almost the entire esophagus. Because of this, a two-stage operative procedure was considered, primarily to intercalate the

colon between the normal esophagus in the neck and the stomach through a mediastinal tunnel without opening the chest, and subsequently to resect the remaining esophagus via a right thoracotomy.

He was operated upon on Jan. 30, 1957. With the child in the supine position the esophagus was exposed in the neck through an incision along the anterior border of the right sternocleidomastoid muscle. A V-shaped segment of the sternum was removed to increase the anterioposterior diameter at the thoracic inlet. This maneuver allows the colon to be displaced into the neck without constriction at this level. The esophagus was transected at the level of the manubrium and a small catheter inserted into the distal end in an attempt to create an external mucus fistula. This was brought out through a stab wound lateral to the original incision. Through a separate abdominal incision, the colon was mobilized in the usual manner. The cecal end was transplanted into the neck through a mediastinal tunnel and an end-to-end esophagocolostomy performed, 2 cm. below the inferior pharyngeal constrictor muscles. The distal end of the viable colonic segment was anastomosed to the stomach and a pyloroplasty was performed. An end-to-end ileocolostomy established lower intestinal continuity. His postoperative course was satisfactory. X-ray examination of the esophagus on March 26 demonstrated narrowing of the esophagocolostomy.

He was readmitted to the hospital on March 26, 1957, because of difficulty in swallowing. Oral ingestion of barium showed an area of narrowing at the level of the seventh cervical vertebra, with no delay in the passage of barium. Attempt at bougienage was unsuccessful and for this reason a revision of the anastomosis was undertaken. Following this, a fistula developed which closed in 12 days. He was admitted again on Aug. 5, 1957, with the same symptoms. A second revision of his esophagocolostomy was carried out, only this time the entire suture line was resected and a re-anastomosis performed with three layers of silk. Dilatations of this anastomosis were carried out at intervals to preclude the development of another stricture.

On June 30, 1958, through a right thoracotomy, the markedly cicatrized esophagus was resected from the cardiac junction to the thoracic outlet. His convalescence was entirely uneventful and he was discharged in good condition on July 12.

He was last seen in the Pediatric Out-Patient Department on April 27, 1959. His weight was 43½ pounds, a gain of 5 pounds in 6 months. The hemoglobin was 12.5 grams with total proteins of 6.4, with albumin of 4 and globulin of 2.5. He had no difficulty in swallowing.

CASE 5.—*Delayed reconstruction for esophageal atresia.*

Baby M was first seen July 1, 1957, at the age of 18 months. His mother stated that he had been operated upon in Germany at the age of 5 days because he could not swallow. Although the original operative record is not available, the fact that the child had a cervical esophagostomy and a feeding gastrostomy suggest that he had a tracheoesophageal fistula with atresia. From observation and physical examination, it was obvious that the baby had received excellent care. Except for the esophageal opening in his neck, a well-healed right thoracic incision, and a gastrostomy tube protruding from the left upper quadrant, no other abnormalities were detected. He weighed 22 pounds and his state of nutrition was good. A recent blood count showed a hemoglobin of 13 grams, hematocrit of 40, a serum protein level of 6.9, with an albumin of 4.2 and a globulin of 2.7. Since the parents were anxious that something be done to restore a swallowing mechanism as soon as possible and since examination disclosed no reason for delay, he was admitted to the hospital for operation on July 11.

With the child in the supine position, the abdomen was opened through an upper midline incision. The ascending and transverse colon were mobilized to the splenic flexure. The right colic artery was temporarily occluded to determine if the middle colic artery could ensure viability of the cecum. The bowel was transected first at the ileocecal junction, the opening in the colon closed, and the appendix removed. The right colic artery and vein were divided close to their origin when it was obvious after 10 minutes of occlusion that the

marginal vessels could provide circulation to the ascending colon through the middle colic artery. The bowel was divided distally near the splenic flexure, thus leaving the segment of bowel suspended upon a vascular pedicle of the middle colic artery and vein. The cervical esophagostomy was dissected from the surrounding tissues and the cecal end of the colon transplanted into the neck through an anterior mediastinal tunnel. The esophagocolostomy was performed with fine interrupted silk and the cologastrostomy with continuous catgut. In this instance, the colon was brought up behind the stomach through the gastrohepatic omentum, as advocated by Haight. This maneuver not only adds length to the segment but it eliminates compression of the duodenum anteriorly by the tenuous middle colic pedicle. The abdomen and neck were closed in the usual manner.

Fig. 3.—Anterior mediastinal colon replacement of the esophagus 2 years following implantation. Although there is slight narrowing in the neck, no obstruction is present.

The child's postoperative course was entirely uneventful. Oral feedings were begun on the ninth day. It was a month, however, before he could swallow in a normal manner. The gastrostomy tube was removed when it became apparent that an adequate oral intake could be maintained.

He was readmitted to the hospital on Dec. 15, 1957, because of progressive dysphagia. A barium swallow demonstrated narrowing in the neck. Dilatation of this area was carried out the following day. On direct endoscopy, the stenosis appeared to be due to angulation at the esophagocolostomy near the thoracic inlet. A No. 33 metal dilator could easily be passed into the colon segment, making it appear that the difficulty in swallowing was due to malposition rather than cicatrization.

Since that time he has been in no real difficulty although an occasional brief episode of dysphagia has been experienced, relieved by a liquid diet for a few days.

A recent blood count disclosed a hemoglobin of 12 grams, red blood count of 4,000,000, with an hematocrit of 38. Total serum proteins were 6 grams, with an albumin of 3.5 and a globulin of 2.5. He is 37 inches tall and weighs 35 pounds. X-ray studies reveal slight narrowing of the lumen in the neck but no obstruction (Fig. 3).

RESULTS AND COMPLICATIONS

To date the colon has been used to reconstruct all or part of the esophagus and stomach in 46 patients for benign or malignant disease. Five of these patients are children who have been followed from 2 to 4 years following colonic implantation. As depicted in Table I, 3 infants had a colon transplant subsequent to corrosive destruction and 2 for esophageal atresia. All are alive and well at the present time.

TABLE I. RESULTS AND COMPLICATIONS

	LESION	OPERATIVE PROCEDURE	COMPLICATIONS	FOLLOW-UP (YEARS)
1.	Tracheoesophageal fistula with atresia	Anterior mediastinal colon transplant	Cervical fistula subsequent stenosis requiring revision and dilatation; no dilatation in the past 1½ years	4
2.	Tracheoesophageal fistula with atresia	Anterior mediastinal colon transplant	Angulation with stenosis which responded to dilatation	2
3.	Corrosive destruction of entire esophagus	Anterior mediastinal colon transplant	Cervical fistula; stenosis requiring revision and dilatation; no dilatation in past 6 months	2½
4.	Corrosive destruction of the lower esophagus	Resection of lower esophagus; intrathoracic replacement with the transverse colon	Abdominal cramps and diarrhea which abated within 2 months	3
5.	Corrosive destruction of the lower esophagus	Resection of lower esophagus; intrathoracic replacement with the transverse colon	Early abdominal cramps and diarrhea	2

In the 2 children in whom the colon was transposed into the neck through an anterior mediastinal tunnel, an anastomotic leak occurred. A subsequent stricture ultimately developed which necessitated revision and dilatation. This is comparable with our experience for high esophageal anastomosis in patients operated upon for carcinoma. In those patients in whom a cervical fistula developed in the early postoperative period, even though this healed readily, a stricture ensued which necessitated either revision or dilatation.

In colonic substitution of the lower esophagus, the complications have been of relatively short duration and have required no further operations. Diarrhea and abdominal cramps have been an early complaint. In 1 boy these persisted for nearly 6 months. During the interim, he was investigated thoroughly at another clinic with negative results. The symptoms are related to the ingestion of food and appear to be some type of gastrocolic reflex. This same symptom complex has been observed in patients following esophagogastrectomy for carcinoma.

DISCUSSION

Although the majority of the colon transplants have been performed in our patients for carcinoma,[1, 7, 15-17] with satisfactory palliation, the operation per se has far wider applicability in children and adults for benign conditions which impair passage of food through the esophagus. The problem of reconstituting an adequate permanent swallowing mechanism in infants with congenital atresia or chemical cicatricial fibrosis has concerned many surgeons.

The colon has many advantages over the stomach and the jejunum. The blood supply is excellent. Due to the anatomic distribution of the marginal arteries, a segment of viable bowel can be mobilized from the cecum to the descending colon if the middle colic artery and vein are left intact. The mucosa is resistant to acid peptic digestion as attested clinically by esophagoscopy and postmortem microscopic examination in patients dying of disease up to 30 months following implantation.[10] Experimentally, the colon transplants in dogs sacrificed up to 9 months showed no evidence of ulceration even though regurgitation was common because of the horizontal position of the animal.[9]

We have been particularly impressed by its length in babies and children. This is due to the redundancy of the transverse colon and the presence of a thin pliable mesentery. Thus, it is an ideal esophageal substitute in congenital atresia or corrosive strictures when long segments are involved.

Although revision and dilatation of the strictured cervical anatomosis was necessary in the 3 children who had an anterior mediastinal colon transplant, they can eat in a normal manner at the present time. It is apparent that, when a cervical fistula develops, the resultant cicatrix will invariably narrow the esophagus sufficiently to cause difficulty in swallowing. When this occurs, an early excision of the suture line with a secondary end-to-end anastomosis is recommended. Angulation of the esophagocolon segment in the neck can be prevented by having the colon lie in a redundant position. In this manner the pharyngoesophagus will not be stretched in a posteroanterior direction around the trachea.

Our original concern over the ability of this colon segment and accompanying vessels to lengthen with the growth of the child has been dispelled. Frequent x-ray examination has demonstrated that the substitute esophagus elongates, commensurate with the growth of the child. Fluoroscopically, regular contractions are evident which propel the bolus along the transplanted colon to the stomach. This, together with a normally placed stomach below the diaphragm, accounts for the excellent nutrition of the infants. None of the patients with high esophagocolostomies exhibits any evidence of colitis or gastritis. The infants in whom the lower esophagus was replaced with the colon have no regurgitation and esophagitis is completely absent. In addition to frequent x-ray evaluation of the esophageal substitute, their general nutritional status is catalogued by weight gain and blood counts. Except for 1 child, who

experienced some gastrointestinal difficulty for 6 months, the weight gain in all patients has been progressive. Hemoglobin, red blood count and serum proteins have all been within normal limits.

SUMMARY

1. The technique for reconstruction of the esophagus in infants with corrosive destruction and congenital atresia is described.

2. The results and complications in 5 children closely followed from 2 to 4 years are presented.

3. The rationale of using the colon in preference to the jejunum or stomach is presented, combined with our experience in 46 patients operated upon for malignant and benign disease.

4. The fact that these children are growing in a normal manner and have no apparent difficulties attest to the fact that the colon can serve as the esophagus both entirely or in part.

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COARCTATION OF THE ABDOMINAL AORTA

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AFTER the first successful operation for coarctation of the aorta by Crafoord in 1945, aortic surgery has advanced at a tremendous rate. In addition to the usual localization in the isthmus of the aorta, a coarctation may be present at any site along the whole course of the vessel. Coarctation of the abdominal aorta is of particular interest, in view of its relation to the celiac, mesenteric, and renal arteries. Altogether 29 such cases have been described earlier.[1-27, 29-31] The coarctation consists either of a stricture involving a segment of varying length, or of hypoplasia of the distal part of the aorta. In 6 of the cases reported in the literature, the aorta was hypoplastic. The stenosis started suprarenally or at the level of the renal arteries in 16 patients, and was situated infrarenally in 11.

The pathogenesis of coarctation of the abdominal aorta is unknown. In a case described by Glenn and his associates,[12] Recklinghausen's disease was present, and caused strangulation of the aorta by neurofibromatous tissue, a situation similar to that found in 1 of our patients.

In the cases reported, the incidence seems to have been the same in both sexes. In 10 patients who died of the disease, the average age was 34 years. Coarctation of the abdominal aorta thus seems to be as serious as coarctation in the isthmus.

Clinically, infrarenal coarctation is characterized by signs of arterial insufficiency, with intermittent claudication, accompanied by moderate hypertension. Suprarenal coarctation produces the same clinical features as those of coarctation of the isthmus, that is, marked hypertension in the upper part of the body, headache, dizziness, and precordial pain. The femoral artery pulse is faint or impalpable. Signs of overloading of the left side of the heart are found, and there is a systolic pressure gradient between the aorta above and below the stenosis. Signs of an increased collateral circulation are sometimes present. A systolic murmur is often audible in the abdomen over the stenosed area. No clinical signs of an impaired blood flow through other organs than the kidneys—for example, the liver, pancreas or intestines—have been described. A definite diagnosis is established by aortography, with injection of contrast medium into the aorta proximal to the stenosis.

Few accounts of surgical treatment of coarctation of the abdominal aorta are found in the literature. Sympathectomy was undertaken in 4 cases, with

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no appreciable effect.[3, 12, 18, 25] In 3 patients with signs of unilateral renal damage, nephrectomy was performed. One patient died, and the condition of the others remained unchanged.[3, 7, 8]

When the renal arteries were not involved in the stenosis, a bypass operation has been performed. Glenn and his colleagues[12] used the splenic artery, after splenectomy, for bypass of a short stenosis directly proximal to the celiac artery. Beattie[5] and Gerbasi[11] and their co-workers performed aorto-aortic bypass with insertion of an homologous vessel graft.

Resection of a membranous stricture between the celiac artery and the renal arteries, with good results, was reported by Gustavino and Becu.[15] Albanese and Baila[2] performed infrarenal resection of the aorta but the patient died postoperatively of anuria.

An account of 3 cases of coarctation of the abdominal aorta in which operation was performed follows.

CASE REPORTS

CASE 1.—The patient was a 12-year-old girl who had had dizziness, headache, and hypertension in the upper part of the body since 10 years of age. The femoral artery pulse was impalpable on either side. The heart was enlarged, with left ventricular hypertrophy. Aortography showed a 6 cm. long coarctation of the abdominal aorta, involving the region of the celiac and superior mesenteric artery and both renal arteries. Distal to the coarctation, the aorta was of normal width.

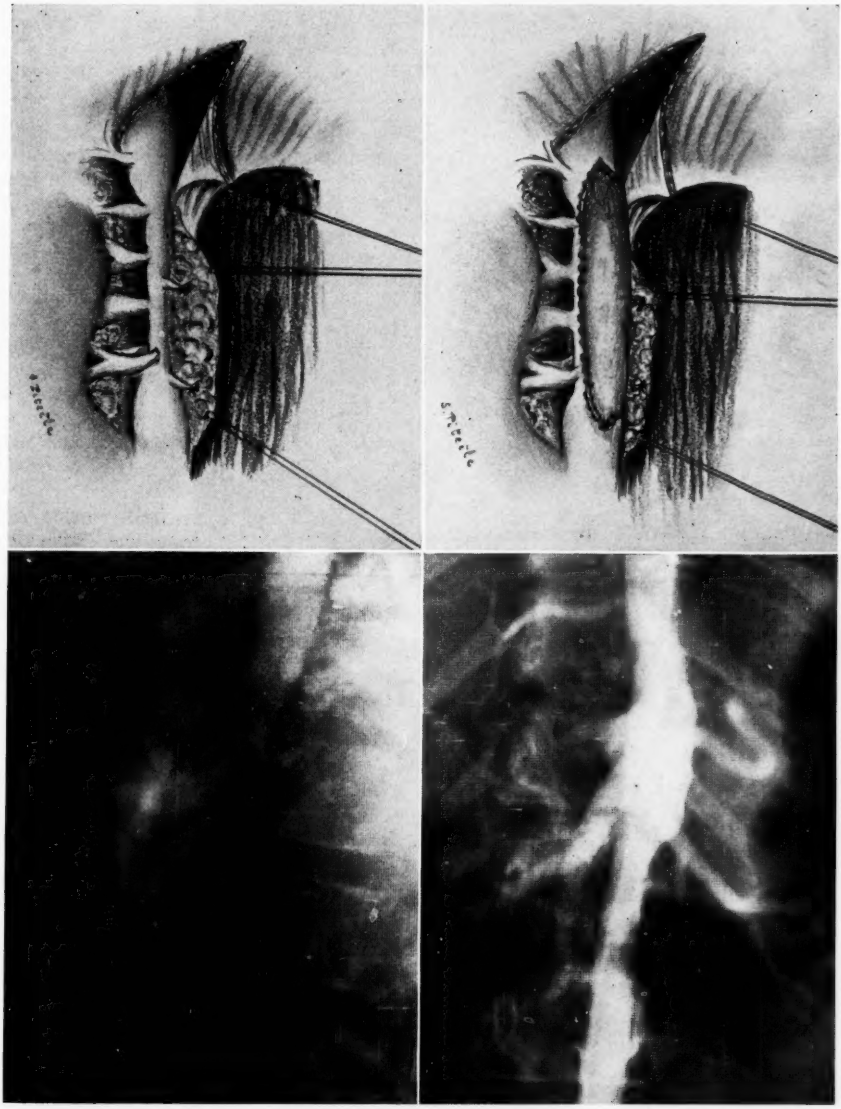
Operation was performed in May, 1957, under hypothermia (28° C.).[16] A thoracoabdominal incision was made at the level of the eighth thoracic vertebra, and the aorta was dissected out retroperitoneally. The stenosed, fibrotically hard, aortic wall was surrounded by abundant periadventitial tissue. This tissue was removed from around the aorta and the origin of the large vessels, and the latter became strongly dilated. At the origin of the renal arteries, their diameter—which was 3 to 5 mm. before operation—was increased to 6 to 8 mm. after dissection. The aorta was split lengthwise for 8 cm. from slightly above the stenosis to slightly below it. A strip-graft,[28] pointed at both ends, of freeze-dried homologous vessel material was sutured into this incision. In view of the patient's age and expected growth, the prosthesis was made 30 per cent larger than the current requirement. Postoperative aortography showed that the diameter of the stenosed segment had increased from 4 to 5 mm. to 20 mm. and that the vessels given off from it were of normal width (Fig. 1).

Operation produced a fall in blood pressure in the upper part of the body from 200/130 to 135/100 mm. Hg, and a rise in the lower part of the body from 125/? to 170/110 mm. Hg. Both femoral artery pulses were distinctly palpable. The heart volume was decreased. Renal function, evaluated by creatinine, para-aminohippurate and inulin clearance was normal, as before operation. At the time of writing (1½ years after operation) the patient is asymptomatic.

CASE 2.—A 25-year-old man with Recklinghausen's disease was found, at 14 years of age, to have arterial hypertension at a routine examination. He had no cardiovascular symptoms. He had the same type of coarctation of the abdominal aorta as the preceding patient, and was operated upon in the same way. A knitted Dacron prosthesis was used as a graft. In this case, the aorta and the origin of the large vessels given off from it were surrounded by abundant, highly differentiated ganglioneuronic tissue. Infrarenally, the aorta appeared somewhat hypoplastic.

The arterial blood pressure in the upper part of the body, which was 180-210/120 mm. Hg before operation, fell to 150/80 mm. Hg after it. However, as can be seen in the

A. *B.*



C. *D.*

Fig. 1.—*A*, Drawing showing coarctation of the abdominal aorta after retroperitoneal mobilization.

B, After removal of periadventitial tissue and insertion of a strip-graft in the posterior aortic wall.

C, Preoperative aortography.

D, Postoperative aortography. The vessels involved in the stenosis are, from below, the renal arteries, the superior mesenteric and the celiac arteries.

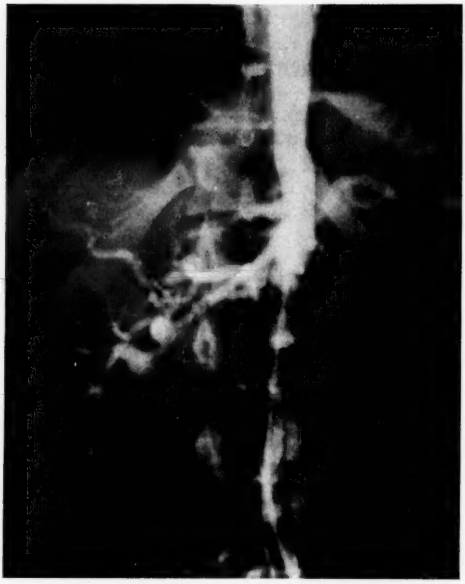


Fig. 2.—Case 2. Postoperative aortography. There is partial stenosis of the left renal artery 2 cm. from its insertion in the aorta, as well as 2 aneurysms of the right renal artery. The aorta is somewhat hypoplastic distal to the coarctation.

Fig. 3.—Thoraco-abdominal, aorto-aortic bypass from 10 cm. above the diaphragm. Dacron graft is sutured distally into an incision in the posterior aortic wall, extending from above the superior mesenteric artery to below the renal arteries.

postoperative aortogram (Fig. 2), a stricture was present in one renal artery, and two aneurysms in the other. Moreover, owing to hypoplasia of the aorta, a systolic pressure gradient of 25 mm. Hg between the thoracic aorta and the femoral artery was still present after operation. The para-aminohippurate and inulin clearance were the same pre- and postoperatively, and renal function was normal in other respects. The patient is asymptomatic and fully fit for work.

CASE 3.—The patient was a 40-year-old woman with arterial hypertension (280/140 mm. Hg). Both femoral artery pulses were faint. Aortography showed coarctation at the level of the diaphragm and slightly above it. Distal to the stenosis, the aorta was occluded by calcium deposits beyond the level of the renal arteries. Infrarenally, the aorta was hypoplastic. Operation consisted of an aorto-aortic bypass with a Dacron graft. The aortic wall proximal to the stenosis was arteriosclerotic and friable. A knitted Dacron prosthesis was sutured end-to-side into the aorta, 10 cm. above the diaphragm. The aorta was split lengthwise at the level of the renal arteries, up to beyond the superior mesenteric artery. The calcium deposits in the aorta were removed, to allow free passage to the renal and superior mesenteric arteries and relatively good passage to the celiac artery. When the Dacron graft, with its distal end cut obliquely, was sutured end-to-side into the aortic incision, the aorta became widened locally (Fig. 3).

Operation produced a fall in blood pressure from 280/140 to 135-175/110 mm. Hg. The femoral artery pulses were stronger. Renal function was normal both before and after operation.

DISCUSSION

Coarctation of the abdominal aorta is a relatively rare disease; only 25 cases have, in fact, been reported during the past 10 years. The prognosis seems to be comparable to that in coarctation of the aortic isthmus, and the indications for operation seem to be the same. The diagnosis is established by aortography, with injection of contrast medium into the descending aorta above the stenosis.

In those cases in which the renal arteries are not involved in the coarctation, surgical treatment presents no great problems. Organs supplied with blood from the large vessels given off from the abdominal aorta other than the kidneys manage by means of collaterals only, with no clinical signs of hypoxia. In such cases, a simple bypass operation can be performed. This has been done earlier, with successful results, in 5 cases reported in the literature. In 1 case, resection could be performed.

When, on the other hand, the renal arteries are involved, the primary aim is to ensure a good blood supply to them. In (the present) Cases 1 and 2, dilatation of the renal arteries, at their origin from the stenosed aorta, was achieved by freeing them from periadventitial and adventitial tissue. The coarctation was then widened by splitting the aorta lengthwise, and inserting a strip-graft from behind.

In Case 3, the renal arteries were given off from the slightly hypoplastic aorta distal to the coarctation, and intra-aortic calcifications, which impeded passage of blood to the renal arteries among other vessels, were also present distal to the coarctation. An aorto-aortic bypass with a graft was therefore performed. The distal end of the graft was cut very obliquely and sutured into a longitudinal incision in the aorta, extending from above the superior mesenteric

artery to distal to the renal arteries (see Fig. 3). When calcified material inside the aorta at the level of the renal arteries and superior mesenteric artery had been removed, the distal end of the graft was sewn into the incision. This resulted in local widening of the aorta, and ensured good passage of blood to the renal arteries.

The blood pressure fell postoperatively in all 3 patients; in Cases 1 and 3 it fell appreciably, whereas the fall was fairly moderate in Case 2. This patient still has a stricture of one renal artery, and two aneurysms of the other.

It has not been possible to establish whether a special renal factor exists, which influences the rise in blood pressure. Renal function was normal both pre- and postoperatively in all 3 cases, and no significant difference in renal blood flow took place.

Since all 3 patients are subjectively healthy postoperatively, it appears that operation is to be recommended. In most cases of coarctation of the abdominal aorta, a bypass operation, performed as in Case 3, would presumably improve the patient's condition, even if the aorta is hypoplastic distal to the renal arteries. In those cases in which the coarctation involves the region from above the celiac artery to just distal to the renal arteries, the strip-graft technique seems to be the method of choice. It relieves the stenosis, and increases the blood flow to the kidneys, as well as to the pancreas, spleen, and other organs.

SUMMARY

An account is given of 3 patients with coarctation of the abdominal aorta operated upon through a thoraco-abdominal incision, and retroperitoneal mobilization of the aorta. In 2 cases a strip-graft technique was used, and, in the third case, aorto-aortic bypass was performed. The results were good in all 3 cases.

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THE SURGICAL CORRECTION OF SYPHILITIC AORTIC INSUFFICIENCY

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DESPITE the numerous operations proposed for the correction of aortic insufficiency, no single procedure has yet evolved which can be effectively and safely applied to the majority of patients in need of assistance. Among the various methods advanced to date, the most widely accepted is the technique of Hufnagel for the placement of a unidirectional flow valve in the descending aorta. When properly done, this operation affords significant palliation and may be a lifesaving measure in selected cases.[1] Unfortunately, this method has serious limitations, exclusive of the operative mortality, as the relief in diastolic reflux is incomplete and at the expense of coronary filling. The indications for this and other operations of a similar nature are not well established and are beyond the scope of this presentation which is a description of a simple and safe means for the correction of aortic insufficiency of syphilitic origin.

The majority of operations for the alleviation of aortic insufficiency are based on the assumption that the aortic valve cusps have been irreparably damaged. This is generally correct with the exception of insufficiency of syphilitic origin.[2] The standard textbooks of pathology describe the events leading to regurgitation as beginning with the spirochetal invasion of the tunica media in the ascending aorta which subsequently undergoes fusiform dilatation.[3] The retrograde extension of this process causes the valve annulus to enlarge symmetrically and functional insufficiency begins with the failure of the valve cusps to coadapt.[2] Progressive regurgitation increases the diastolic capacity of the ventricle with further annular widening, and the fatal cycle is established. The valve cusps undergo fibrotic changes with some nodular thickening and the adjacent aortic wall shows intimal thickening which may cause narrowing of the coronary ostia.[4] This latter change is said to be the cause of the anginal syndrome with eventual myocardial failure. To ascertain the effect of these changes on valve function, a number of syphilitic hearts were studied and it was apparent that the cusps had suffered little loss of motility and the coronary ostia were only slightly narrowed. These observations formed the basis of a new concept for treatment of aortic insufficiency, which consists of plication of the aortic annulus rather than the use of substitute valvular prosthesis. A study of fresh hearts demonstrated the feasibility of this approach

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which consists of the circumferential dissection of the root of the aorta and isolation of the coronary vessels allowing for the placement of an external ligature at the level of the annulus, passing below the left and just above the right coronary artery. Controlled plication should diminish or abolish regurgitation without impingement on the coronary vessels or production of outflow obstruction. The degree or amount of narrowing is easily determined by means of continuous pressure recordings from the left ventricle and aorta. After

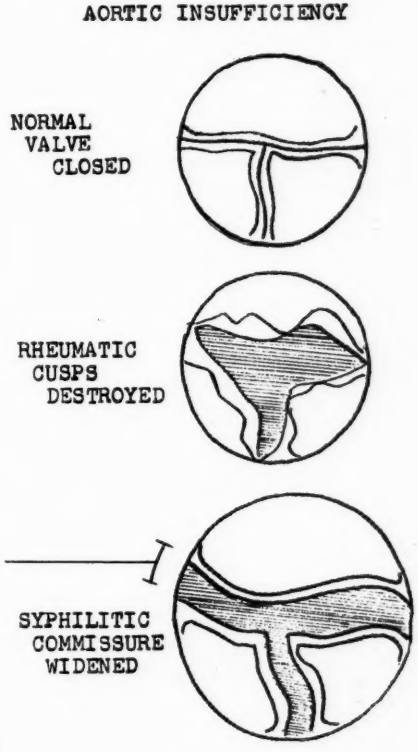

Fig. 1.

proper placement of the ligature, constriction is carried to that point where the diastolic pressure enters the normal range without production of a systolic gradient across the aortic valve area. The simplicity of this procedure is further enhanced by the ready accessibility of the aortic root through a median sternotomy which avoids the violation of either pleural cavity.

The case report which follows is a description of the first clinical application of this technique.

CASE REPORT

On May 1, 1959, a 59-year-old white man was admitted to St. Joseph's Hospital for treatment of intractible heart failure secondary to aortic insufficiency of syphilitic origin.

The initial diagnosis of neurovascular syphilis had been made 10 years previously, at which time active antisyphilitic therapy was carried out. Examination revealed bilateral primary optic atrophy with neurogenic bladder and an aortic insufficiency of moderate degree in a compensated myocardium. The first symptoms of left ventricular failure did not appear until 6 months before hospitalization. At that time, medical therapy was begun with marked symptomatic relief until 1 month before admission when nocturnal dyspnea developed with anasarca and other signs of advanced congestive heart failure.

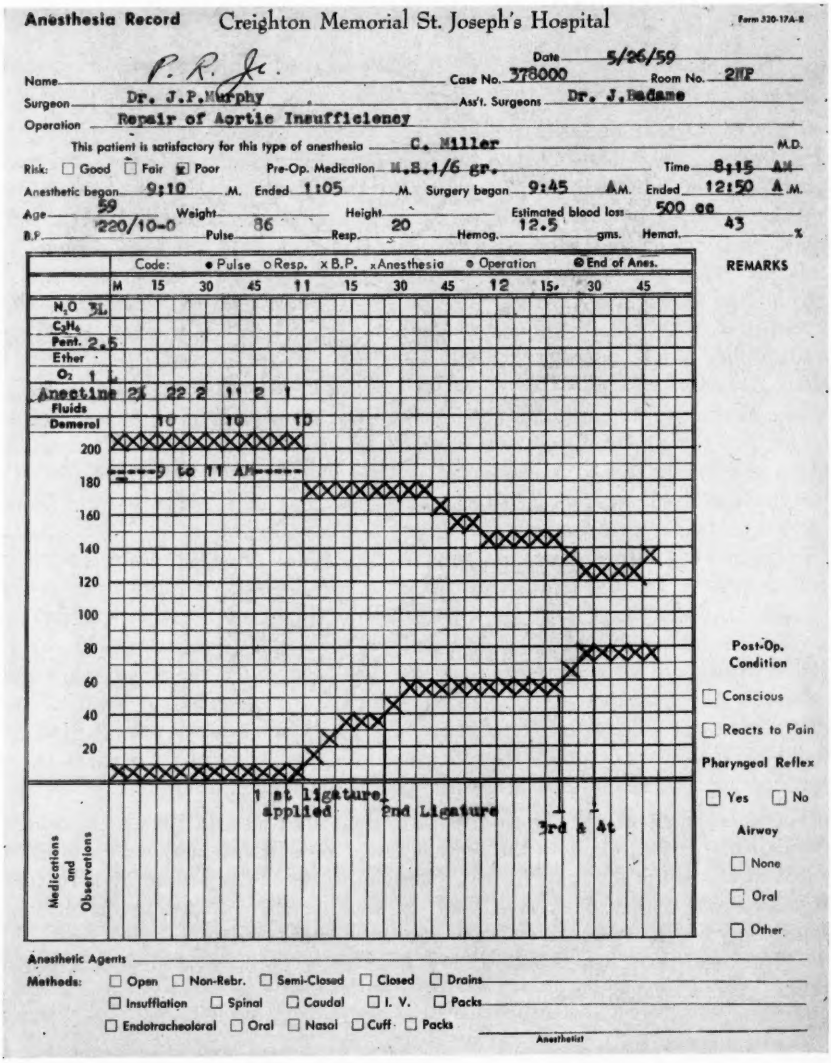

Fig. 2.

Intensive cardiac treatment with digitalis and diuretics failed to alter the downhill course and the patient required continuous oxygen therapy.

Physical evaluation revealed a blood pressure of 220/0 mm. Hg in both arms with all the classical signs of extreme aortic regurgitation manifest in the peripheral pulses. There was a massive precordial heave with extreme cardiomegaly. A Grade 5 aortic diastolic murmur was present with a soft short systolic blow. Cardiac fluoroscopy revealed a linear calcification of the aortic arch with a large heaving left ventricle. The electrocardiogram showed left ventricular hypertrophy and strain.

Despite the extreme dyspnea, the patient's chief complaint was the constant pulsatile body motion which shook the bed with each heartbeat.

On May 25, surgical consultation was secured in order to consider the insertion of a Hufnagel valve. This approach was rejected because of the intractable heart failure. However, as death was imminent it was elected to undertake plication of the aortic annulus.

Surgery, carried out on May 25, consisted of isolation of the aortic root through a median sternotomy. On opening the pericardium, the left ventricle and ascending aorta were found to be massively enlarged. The coronary vessels and the right heart were not abnormal. A direct pressure from the brachial artery was 220/10 mm. Hg. Catheters placed in the aorta gave an identical reading and left ventricular pressure averaged 210-200/15-10 mm. Hg. Pressures taken by cuff over the left brachial artery were identical to the aortic pressure. The base of the annulus was dissected circumferentially and an umbilical tape was passed along this tract coursing below the left or posterior coronary artery and above the right. Progressive narrowing of the tape was caried out until the diastolic pressure reached 40 mm. Hg. The systolic pressure fell simultaneously from 220 to 140 mm. Hg. After securing the knot, a second and a third tape were passed over the same tract and narrowed until the diastolic pressure reached 80-70 mm. Hg. At this point, the systolic reading was 120 mm. Hg in the aorta and left ventricle (Fig. 2). These pressures were considered an endpoint, having restored a normal blood pressure without producing an aortic stenosis. The patient's condition remained good throughout the entire procedure and no arrythmias were noted. The sole alarming feature was the post-plication appearance of the aortic root which was reduced to normal size at the valve but massively dilated above this point. This abrupt transition in caliber was accompanied by a systolic thrill which was not present before surgery and doubtless represented the turbulent change in a post-stenotic dilatation. In this instance the stenosis did not represent physiologic obstruction.

The postoperative course was complicated by a minor wound disruption but otherwise was uneventful. The diastolic murmur was no longer heard but was replaced by a soft systolic component. All signs of heart failure rapidly disappeared as did the pulsatile body motion. For this last relief, the patient was most grateful. On release from the hospital, brachial pressures averaged 140/80-60 mm. Hg. Five months later, pressures averaged 160-140/85-75 mm. Hg. The patient is free of all signs and symptoms of heart failure and has not received any cardiac therapy since leaving the hospital. X-ray studies show a significant diminution in the cardiac silhouette, although some left ventricular hypertrophy remains. The electrocardiogram has undergone a marked change; there is loss of the strain pattern, although some left heart hypertrophy is apparent.

SUMMARY

The pathologic abnormality resulting in aortic regurgitation secondary to syphilitic aortitis does not necessarily involve a loss of valve substance or cusp motility but, rather, consists primarily of a dilatation of the aortic annulus.

Restoration of valvular competence is best accomplished by plication of the annulus rather than the use of valve prothesis.

A simple and safe technique for annular plication is described, together with a summary of the first clinical application with this method.

ADDENDUM

The patient was examined 13 months after the operation. His condition remains excellent.

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THE EFFECT OF TOTAL BODY PERFUSION UPON CARDIAC OUTPUT AND VASCULAR RESISTANCE

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INTRODUCTION

HYPOTENSION usually follows extracorporeal perfusion in animals and is also observed in patients. Previous work from this laboratory[1] demonstrated that decreased peripheral flow and vascular resistance play a part in this post-perfusion decrease in systemic pressure. As a continuation of this study, the following experiments were carried out in order to determine the relative roles of cardiac output and total body vascular resistance in hypotension following cardiopulmonary bypass.

METHODS

Healthy mongrel dogs, weighing between 14.0 and 19.5 Kg., were anesthetized with intravenous thiamylal, 12.5 mg. per kilogram. Following intubation, respiration was maintained with an intermittent positive pressure respirator using room air. The left chest was opened through the fifth intercostal space, No. 20 Fr. catheters were inserted into the venae cavae, and the left femoral artery was cannulated. Heparin, 12 mg. per kilogram, was given intravenously. The descending aorta was cross-clamped for less than 2 minutes and a Gregg-type rotameter[7] was inserted just distal to the left subclavian artery. The brachiocephalic and left subclavian arteries were cannulated and connected to the distal limb of the rotameter in such a way that the cerebral blood supply was never completely interrupted. Thus, the entire cardiac output was directed through the flow meter, with the exception of coronary flow. Mean arterial, central venous, and left ventricular pressures were measured with strain gauge transducers and recorded simultaneously with electrocardiogram and cardiac output on a photographically recording oscilloscope. The rotameter was calibrated with blood from the extracorporeal system at the conclusion of each experiment.

Total vascular resistance was calculated by dividing the mean aortic pressure in millimeters of mercury by the cardiac output in cubic centimeters per minute and multiplying the dividend by 100.

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TABLE I. CARDIAC OUTPUT AND AORTIC PRESSURE BEFORE AND AFTER CONTROL AND PERFUSION PERIODS

	EXPT. NO.	PRESSURE (MM. Hg)				CARDIAC OUTPUT (C.C./MIN.)			
		CONTROL		PERFUSION		CONTROL		PERFUSION	
		BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
High Flow Rate (100 c.c./Kg./min.)	176	75	74	76	72	340	750	420	200
	178	89	88	90	55	850	650	1,400	400
	185	88	88	90	71	925	775	1,000	400
	188	77	90	84	55	1,475	1,500	1,280	780
	189	79	103	100	60	1,320	1,200	1,200	900
Mean ± S.D.*		82 ± 6	89 ± 10	88 ± 9	63 ± 8	980 ± 450	975 ± 400	1,060 ± 385	535 ± 290
Low Flow Rate (50 c.c./Kg./min.)	179	65	70	70	56	400	400	500	475
	180	68	75	69	36	900	700	960	250
	181	74	80	102	35	550	475	850	150
	183	86	91	79	40	890	1,190	1,100	550
	186	88	90	90	65	625	590	700	400
Mean ± S.D.		76 ± 10	82 ± 9	82 ± 14	56 ± 20	675 ± 215	670 ± 310	825 ± 170	365 ± 165
Mean ± S.D. (combined experiments)		79 ± 9	85 ± 10	85 ± 11		830 ± 370	830 ± 355	940 ± 345	

*Standard deviation.

$$\text{Total Vascular Resistance} = \frac{\text{Mean Aortic Pressure}}{\text{Cardiac Output}} \times 100.$$

This abbreviated Poiseuille's equation yields a number which indicates relative degrees of vascular resistance. Since a linear relationship between pressure and resistance does not obtain,[5] resistances were compared at equal pressures for purposes of accuracy.

Cardiac output was recorded and total vascular resistance calculated at various arterial pressures before and after a 30-minute pre-perfusion control period. Similar measurements were made after a 30-minute perfusion period. Arterial pressures were varied during these experimental periods by adding or removing blood from the animal.

Cardiopulmonary bypass was carried out utilizing 100 per cent oxygen in a rotating disk oxygenator, previously primed with 2,500 c.c. of freshly drawn, heparinized blood. Five animals were perfused at rates of 100 c.c. per kilogram per minute (high flow group) and 5 animals at rates of 50 c.c. per kilogram per minute (low flow group). Since blood lost from the operative field was returned to the extracorporeal circuit, by comparing the pre- and post-perfusion circuit volume, the amount of blood lost or pooled by the animal was determined.

Venous and arterial blood samples were drawn at the beginning and end of the perfusion period and analyzed for packed cell volume, pH, oxygen and carbon dioxide content. Oxygen and carbon dioxide content were determined by the method of Van Slyke and Neill,[10] and carbon dioxide tension was calculated using the normogram of Van Slyke and Sendroy.[11]

RESULTS

Detailed data obtained in individual animals during the various experimental periods are reported in Table I (cardiac output and arterial pressure) and in Table II (total vascular resistance). These tables may be referred to for specific data but the results are summarized in Tables III through V and Fig. 1. Since cardiac output, aortic pressure, and total vascular resistance did not change significantly during the pre-perfusion control period in any of the ten experiments, they were combined and listed as a single control group in Fig. 1 and the tables summarizing the results.

In all 10 animals, hypotension followed extracorporeal perfusion (Table III). In the high flow group, the average pressure fall was from 85 mm. Hg before perfusion to 63 mm. Hg following perfusion. In the low flow group, the average pre-perfusion pressure was 85 mm. Hg, falling to 56 mm. Hg immediately after perfusion.

Cardiac output (Table IV) in the high flow group fell from a pre-perfusion level of 940 to 535 and in the low flow group from 940 to 365 c.c. per minute in the immediate post-perfusion period. The decreases in pressure and output as a result of bypass are statistically significant as indicated in Tables III and IV.

Table V shows the effect of perfusion upon total body vascular resistance. Resistance did not change significantly in the high flow group as compared to control values. But on the other hand, resistance was significantly reduced below control levels following low flow perfusion.

TABLE II. PER CENT CHANGE IN RESISTANCE FOLLOWING CONTROL AND PERFUSION PERIODS

	EXPT. NO.	% CHANGE IN RESISTANCE	
		CONTROL PERIOD	POST-PERFUSION
High Flow Group (100 c.c./Kg./min.)	176	− 1	+82
	178	+23	+33
	185	+42	+24
	188	− 9	+25
	189	+26	−36
Mean ± S.D.*		+16 ± 20	+26 ± 45
Low Flow Group (50 c.c./Kg./min.)	179	− 7	−30
	180	+ 3	−36
	181	+ 9	−48
	183	—	—
	186	+12	−30
Mean ± S.D.		+4 ± 8	−32 ± 3
Mean ± S.D. (combined experiments)		+11 ± 17	

*Standard deviation.

TABLE III. EFFECT OF PERFUSION ON ARTERIAL PRESSURE

	PRESSURE (MM. Hg)			
	COMBINED CONTROL		PERFUSION	
	BEFORE	AFTER	BEFORE	AFTER
High Flow			85 ± 11	63 ± 8
				$p < 0.001$
	79 ± 9	85 ± 10		
Low Flow			85 ± 11	56 ± 20
				$p < 0.002$

TABLE IV. EFFECT OF PERFUSION ON CARDIAC OUTPUT

	CARDIAC OUTPUT (C.C./MIN.)			
	COMBINED CONTROL		PERFUSION	
	BEFORE	AFTER	BEFORE	AFTER
High Flow			940 ± 345	535 ± 290
				$p < 0.02$
	830 ± 370	830 ± 355		
Low Flow			940 ± 345	365 ± 165
				$p < 0.001$

TABLE V. EFFECT OF PERFUSION ON TOTAL VASCULAR RESISTANCE

	% CHANGE IN TOTAL VASCULAR RESISTANCE	
	CONTROL PERIOD	POST-PERFUSION
High Flow		+26 ± 45
		$p < 0.003$
	+11 ± 17	
Low Flow		−32 ± 3
		$p < 0.001$

A graphic presentation of the effect of perfusion upon cardiac output, aortic pressure, and total vascular resistance is shown in Fig. 1. This graph clearly shows, as indicated above, that there is a significant fall in aortic pressure and cardiac output following either high or low flow cardiopulmonary bypass. Total vascular resistance on the other hand, rises somewhat (not significantly) following high flow perfusion, but falls following one-half hour of perfusion at 50 c.c. per kilogram. This graph also demonstrates that during the 30-minute period of observation before perfusion, the animals were all quite stable.

EFFECT OF PERFUSION ON AORTIC PRESSURE, CARDIAC OUTPUT, AND TOTAL VASCULAR RESISTANCE

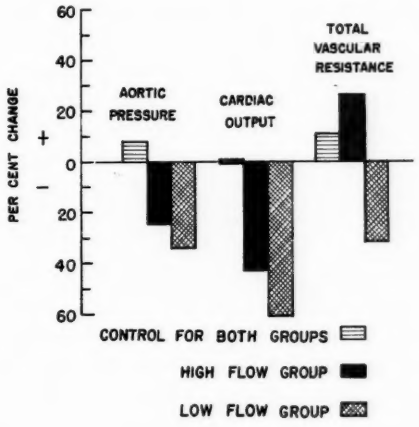

Fig. 1.

Both groups of animals were comparable as regards pH, arterial and venous oxygen saturation, arterial carbon dioxide tension, and hematocrit at the end of perfusion. Eight of 10 dogs pooled blood during perfusion, the high flow group tending to pool more blood than the animals in the low flow group. In no experiment was there a significant elevation of central venous pressure or left ventricular end diastolic pressure.

DISCUSSION

Previous measurements of resting cardiac output in closed chest dogs have been in the range of 100 c.c. per kilogram per minute.[4, 9] In our experiments, cardiac output was measured in anesthetized animals prepared for cardiopulmonary bypass and was found to be in the range of 50 c.c. per kilogram per minute. This latter figure is comparable to cardiac output in open heart preparations reported elsewhere,[2, 4, 6, 8] and can probably be explained by loss of negative intrathoracic pressure[3] and the trauma of surgery, including blood loss, catheters in the venae cavae, and vascular reflex changes.

Hypotension followed perfusion in all 10 animals and was primarily due to a decrease in cardiac output. This decreased cardiac output could be the result of (1) myocardial failure or (2) a decreased effective circulating blood volume. Cardiac failure did not appear to be a factor, since at no time was there any elevation of left ventricular end diastolic or central venous pressure.

Therefore, a decreased effective circulating blood volume was probably responsible for this diminished cardiac output. Consistent with this conclusion is the fact that all animals responded to transfusion of small amounts of whole blood by increasing cardiac output and aortic pressure toward control levels. This diminished blood volume is not the result of external blood loss but is probably due to the fact that the animals pooled sizeable quantities of blood during perfusion. This blood absorbed by a perfused animal must be sequestrated in inaccessible vascular pools. Work in progress in our laboratory indicates that the liver is one of the sites for this blood sequestration.*

Decreased post-perfusion total body vascular resistance also contributed to hypotension in the low flow group whereas the animals perfused at their estimated resting cardiac output (100 c.c./Kg./min., high flow group) were able to maintain their vascular resistance. There were no differences in body temperature, pH, arterial or venous oxygen saturation or arterial carbon dioxide tension between the high and low flow groups to account for this fall in resistance.

The results of these experiments have definite clinical application. First, the fact that low perfusion flow rates result in a loss of vascular tonus emphasizes the importance of maintaining as high a perfusion rate as possible during cardiopulmonary bypass. Furthermore, these experiments show that hypotension following cardiopulmonary bypass is a result of decreased cardiac output due to a diminished effective circulating blood volume. With this experimental evidence in mind, we have found that, following total cardiopulmonary bypass, it is often necessary to discontinue perfusion with a positive blood balance in order to maintain an adequate systemic pressure. In fact, if hypotension is present, blood is given to the patient until the right atrium appears to be slightly distended. In almost every instance, the infusion of additional blood results in maintenance of a normal systemic pressure and adequate cardiac output. If the pressure does not respond to this additional volume of blood before the atrium becomes too distended, vasopressors are then indicated. We have not found it necessary to use vasopressors to maintain systemic pressure in the last 100 clinical cases.

SUMMARY

1. Cardiac output, aortic, left ventricular and venous pressures were measured during 30 minutes of control and after a half-hour period of extracorporeal bypass in animals.

*To be published.

2. In 5 animals (high flow group), arterial perfusion rate was 100 c.c. per kilogram per minute and, in 5 animals (low flow group), the rate was 50 c.c. per kilogram per minute.

3. Hypotension and decreased cardiac output followed perfusion in all animals.

4. This hypotension and decreased cardiac output are probably due to a decreased effective circulating blood volume as a result of blood pooling.

5. Perfusion rate of 50 c.c. per kilogram per minute resulted in a decrease in total body vascular resistance, but resistance remained unchanged following high flow perfusion rate.

6. The results of these experiments emphasize the importance of maintaining high flow rates and explain the rationale for maintaining a positive blood balance following extracorporeal bypass.

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AUTOGENOUS OXYGENATION WITH CARDIAC BYPASS, HYPOTHERMIA, AND AN ATRIOVENTRICULAR CLAMP

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THE RECENT REBIRTH of interest in autogenous oxygenation with bypass during cardiac surgery is the natural product of a desire to achieve the ideal method of cardiac isolation.

We have used autogenous oxygenation with rapid cooling to allow cardiotomy at low temperatures while perfusion is stopped[12] and now present a method that permits cardiotomy during autogenous oxygenation without interruption of perfusion. This system depends upon the use of a clamp which interrupts blood flow at the atrioventricular level.

There have been a number of other attempts in the past to use autogenous oxygenation for intracardiac surgery. In 1950, Sirak[13] employed experimental left atrial cannulation with a diaphragm occlusion of the mitral valve to provide a bloodless left ventricle. Since then numerous investigators, notably Potts,[10] Wesolowski,[14] Cohen,[4] Campbell,[3] Read,[11] and more recently Blanco,[1] Mustard,[9] Helmsworth,[7] Shields and Lewis,[12] and Drew[5, 6] and their associates have attempted to utilize the natural medium of oxygenation for open-heart surgery. Their results have varied considerably, with the most consistent problems involving left atrial drainage, pulmonary edema, the need for intracardiac catheters, and difficulties in producing dry intraventricular fields.

Our present study on this subject was directed toward further perfection of the technique of bilateral cardiac bypass and determination of the maximum safe period of ventricular ischemia with the use of a special atrioventricular clamp, profound hypothermia, and autogenous oxygenation.

MATERIALS AND METHODS

A total of 50 adult mongrel dogs, whose average weight was 30 pounds (13.6 Kg.), were subjected to cardiac bypass under Sodium Pentothal (27.5 mg./Kg.) anesthesia and artificial ventilation with 100 per cent oxygen.

Thoracotomy was performed through the fourth left intercostal space and after heparinization (2 mg./Kg.), cannulations shown in Fig. 1 were carried

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out. The pulmonary artery was cannulated approximately 1.5 cm. distal to the pulmonary valve using a double purse-string suture and a 16 Fr. catheter (Fig. 2). The right and left atria were cannulated via the auricular appendages using 24 Fr. Bardic catheters with multiperforated steel inserts (Fig. 4, *d*). A 14 to 16 Fr. catheter was inserted in the femoral artery.

On completion of the bypass, 100,000 units of penicillin was injected into the free pleural cavity. A chest tube drainage was used for 2 to 3 hours. Postoperatively, intramuscular injections of 100,000 units of penicillin were given daily for 3 to 4 days.

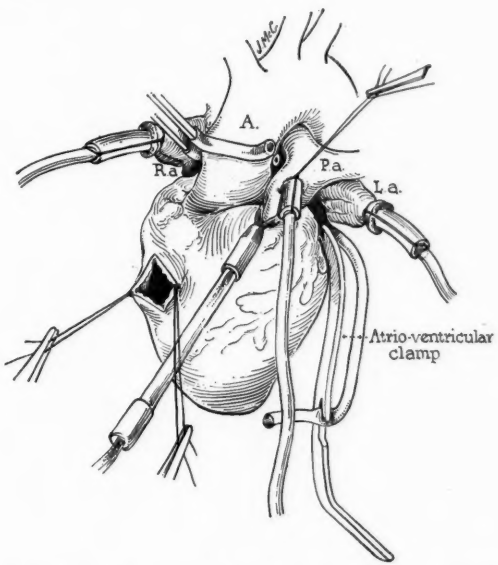

Fig. 1.—Drawing which shows cannulated heart during total bypass and ventricular isolation. Atrioventricular clamp is seen compressing both inflow tracts on atrial side of A-V groove. Femoral artery cannula is not pictured.

Two identical pump bypass units,[8] similar to those described previously,[12] were used (Fig. 3). Sealed plastic bag reservoirs were used instead of open Lucite cylinders. The distensibility of the plastic bags allowed the use of a simple volume detector which activated a relay system to operate the blood pumps, thus providing semi-automatic control which permitted the use of a small extracorporeal blood volume (600 c.c.). De Bakey or Sigmamotor pumps were used. Each pump unit was primed with 300 c.c. of fresh heparinized whole blood (30 mg. per liter). Following the bypass, the heparin was neutralized by intravenous injection of Polybrene (1 mg. for each milligram of heparin given prior to bypass).

In the first 15 experiments, cooling and rewarming was accomplished by the immersion of two 15 feet coils of stainless steel tubing interposed, one in each pump circuit, in pails of salt-ice-water solution (0° C.) followed by warm water (45° C.).

The 35 remaining experiments were conducted using a Brown-Sealy blood heat exchanger[2] which cooled either the systemic or pulmonic circuits. The temperature of this device was regulated by the circulating fluid of an Autotherm* machine. This device integrates electronically the subject's temperature with a variable desired temperature to cause the circulating fluid to cool or warm the subject to the desired temperature. The minimum cooling fluid temperature was 6° C., while the maximum warming temperature was 44° C. Rewarming was aided by use of a Therm-O-Rite blanket at 46° C.

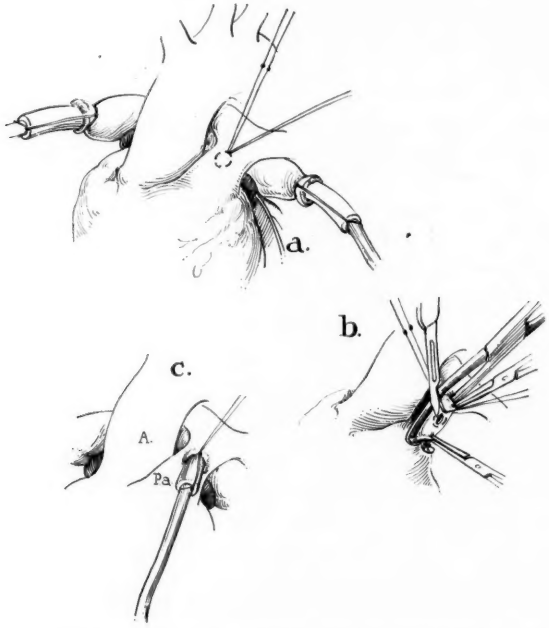

Fig. 2.—Drawing which shows steps in cannulation of pulmonary artery.

a, Double-stranded purse-string suture in pulmonary artery.

b, After hemostat traction on pulmonary artery adventitia, a Beck aorta-type clamp is applied to isolate purse string in pulmonary artery. An arteriotomy is then made as shown and the cannula is inserted.

c, One strand of purse string is tied to anchor cannula. Remaining purse string is tied following removal of cannula to close arteriotomy with negligible stenosing.

In several experiments the pleural cavity was irrigated with cold (6 to 10° C.) saline to accelerate the cooling rate and to provide local heart cooling.

Isolation of both ventricles was achieved by occlusion of inflow and outflow tracts. The inflow occlusion was simple and by allowing uninterrupted filling of the atria could be continued during ventriculotomy or aortotomy. This inflow occlusion was accomplished by applying tension to a rubber tube lying within the transverse cardiac sinus and attached at one end to a metal bar which was in contact with the atria posteriorly in the oblique sinus. The free end

*Autotherm Corp., West Los Angeles, Calif.

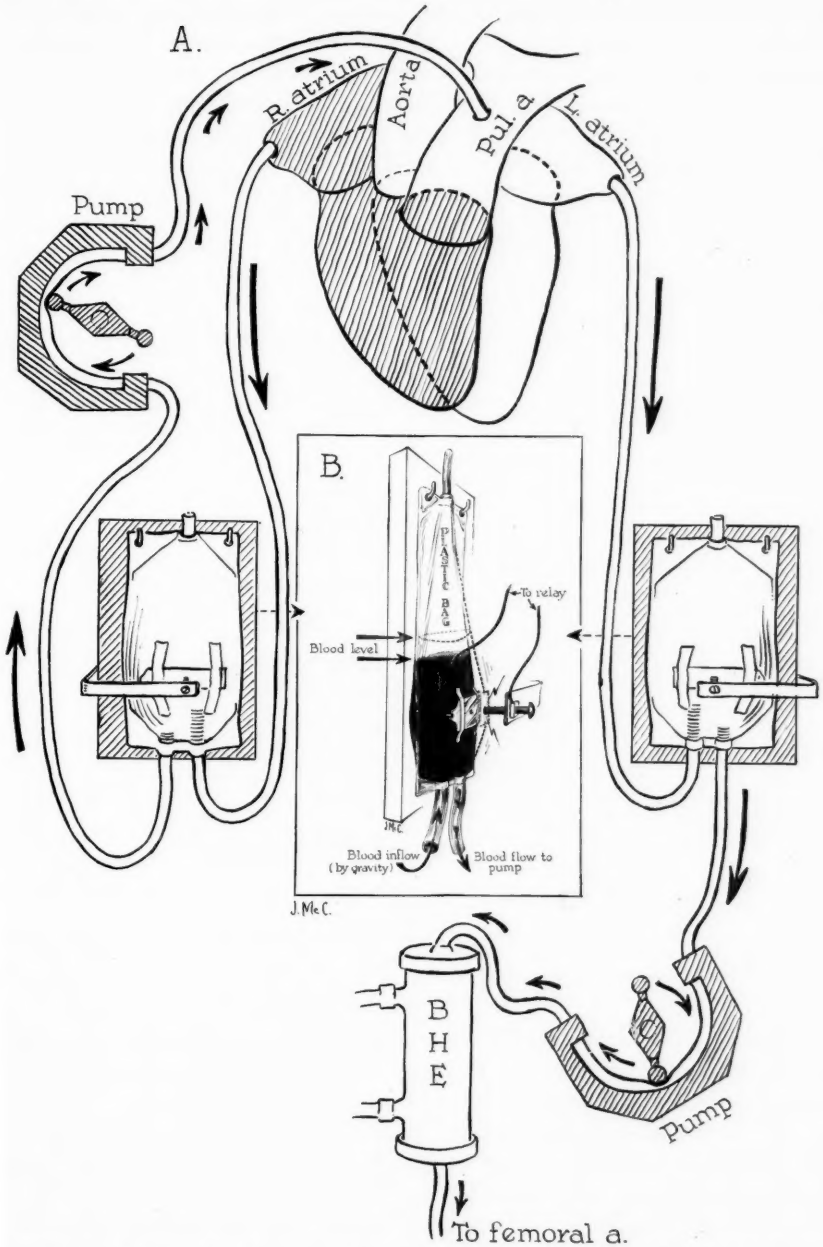

Fig. 3.—*A*, Schematic drawing of bypass system with two pump units showing plastic bag reservoirs with attached volume detector, automatically controlled pumps, and blood heat exchanger.

B, Detailed drawing of reservoir and volume detector.

of the rubber tube was then anchored in a notch in the metal bar, resulting in complete occlusion of the atria on the atrial side of the coronary sulcus without serious limitation of the atrial capacities (Fig. 4, *b* and *c*).

Following inflow occlusion, the ascending aorta was cross-clamped with a clamp of the Blalock type. The pulmonary artery was occluded proximal to the catheter with a rubber-tipped glass tube umbilical tape tourniquet. A right ventriculotomy was performed in all cases to ascertain the effectiveness of the inflow clamp.

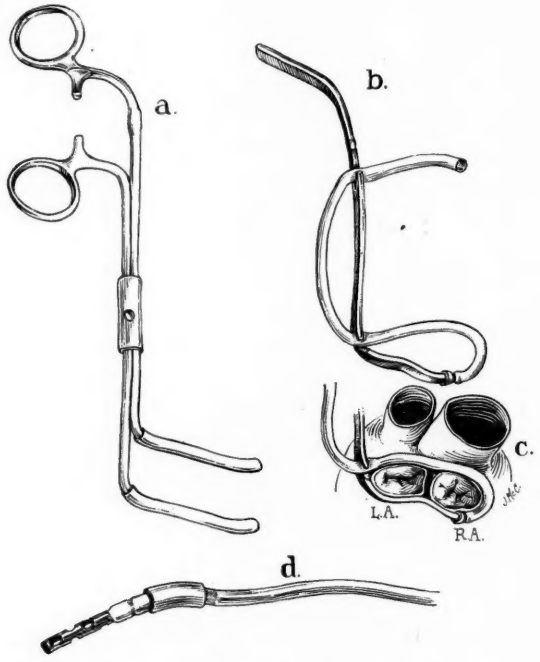

Fig. 4.—*a*, Rubbed-sleeved compression atrioventricular clamp.
b, Rubber tube traction atrioventricular clamp.
c, Clamp *b* applied around atria.
d, Atrial cannula with multiperforated metal insert.

Atrial occlusion was accomplished when the heart temperature was below 25° C. in the hypothermia experiments. Rewarming was started 10 to 15 minutes before occlusion was released.

In the group of 6 normothermic dogs, cardiac arrest was obtained by injecting potassium citrate solution (4 dogs) or acetylcholine (2 dogs) proximal to the aortic clamp.

Monitoring catheters were routinely inserted into the femoral artery and vein and left atrium for direct pressure readings. Temperatures of the rectum, heart, esophagus, circulating blood in the bypass and Autotherm fluid were

recorded. Flow rates of bypass pumps and amounts of blood and saline given during the procedure were also recorded.

Blood samples were drawn for control studies, following the cooling stage, before discontinuing the bypass, and 2 to 3 hours postoperatively. Plasma hemoglobin and pH studies were performed on each sample. In 40 per cent of the experiments, hematocrit, CO_2, pCO_2, O_2 content and per cent of O_2 saturation determinations were taken.

Dogs surviving over 1 week were considered long-term survivors. All dogs were autopsied and specimens were taken for histologic studies.

RESULTS

The 50 experiments were divided into five groups according to the length of ventricular isolation and the blood circuit used for temperature control. The groups of experiments were done in sequence, A through E. The results are summarized in Table I.

TABLE I

	GROUP					
	A	B	C	D	E	TOTAL
Time isolation (min.)	30	30	45	45	60	
Total length of bypass	56 min. 43-62	42 min. 39-48	75 min. 64-85	64 min. 56-72	76 min. 67-85	
Circuit cooled	Both	Normothermic	Systemic	Pulmonic	Systemic	
Number of dogs	15	6	11	7	11	50
Technical deaths	0	1	0	2	2	5
24-hour survivors	11 (74%)	5 (100%)	8 (73%)	4 (80%)	3 (33%)	31 (70%)
7-day survivors	10 (67%)	3 (60%)	8 (73%)	2 (40%)	1 (11%)	24 (53%)
Average heart temp. during cooling	16° C.	32° C.	19° C.	20° C.	20° C.	
Average arterial pressure during bypass (mm./Hg)	82	100	79	80	73	
Average perfusion rate (c.c./min./Kg.)		90	60	70	50	

It will be seen that the mortality was similar at 30 and 45 minutes of ventricular isolation, with an increase in mortality as 60 minutes of isolation was reached. Thirty minutes of cardiac isolation with this system was tolerated quite well even at normal temperature, but 60 minutes resulted in a high mortality rate even with hypothermia added. This may simply indicate that

we had reached the limit at which cardiac recovery from ischemia was impossible. In most cases, perfusion of the rest of the animal seemed adequate.

Results of the 50 experiments will be described in the following five categories:

1. *Deaths.*—The five technical deaths in this study resulted from pump or respirator failure. Primary findings in nontechnical deaths were 6 hemothorax, 5 shock, 5 pulmonary complications, 2 neurologic complications, and 3 undetermined. Over half of the deaths from hemorrhage and shock were in the first group during procedure development and in the 60-minute occlusion group. Those succumbing to pulmonary complications were in the normothermic and pulmonary cooling groups.

2. *Pathology.*—The most consistent gross pathologic features seen in the autopsied hearts were organized atrial thrombi along the line of clamp compression in 8 of the 24 long-term survivors and myocardial ecchymosis along the same line in most short-term survivors. These findings were especially marked in the atria clamped with parallel rubber-sleeved metal bars (Fig. 4, *a*) which were used in the early experiments.

Other findings among long-term survivors included myocardial abscesses in 4 dogs, four empyemata, and three single lobe atelectases. Death apparently due to pneumonia in 1 dog was the only known instance of fatality from infection. All 5 dogs in Group B (normothermic occlusion), showed a transition of diffuse red hemorrhagic to brownish discoloration of the ventricular myocardium, depending upon the length of survival.

Hind limb paralysis was noted in 2 short-term survivors. The primary cause of death was not determined.

Histologic study of sections taken through the area of atrial compression revealed fibrous organization in the regions of subendocardial ecchymosis. Liver, lung, and kidney sections showed no consistent pathology and did not help in determining the cause of unexplained deaths.

3. *Blood Pressure.*—Venous and atrial pressure recordings indicated that adequate drainage of both atria can be accomplished with a resultant arterial pressure compatible with life.

Venous (inferior vena cava) pressures showed a consistent pattern. Following occlusion, the pressure would rise approximately 4 cm. of saline and then slowly return to normal or often 3 to 4 cm. below on termination of the bypass.

Pulmonary artery pressures were taken in several instances in Group A and did not exceed 25 mm. Hg during occlusion.

Results of left atrial pressure monitoring indicated that the gravity drainage was adequate, since there was seldom more than a 5 cm. saline pressure increase during occlusion period. On numerous occasions the pressure fell below normal, especially during the last 15 minutes of occlusion in the 45- and 60-minute groups. A potential hazard was seen in the occasional occurrence

of a negative left atrial pressure following release of occlusion. In such situations we felt the avoidance of air embolism from a loosely fitting catheter was accomplished by using a double looped 1-0 silk suture tied around the atrial appendage and its contained catheter with an internal supporting metal insert (Figs. 1 and 4, *d*).

The arterial pressure pattern was quite similar in all experiments except the normothermic group. There was a 20 to 30 mm. Hg pressure drop during the cannulation period. A further 30 to 40 mm. Hg drop was seen during the first 5 minutes of the bypass with cooling. The pressure would then rise in response to fluid administration and would remain reasonably constant for 15 to 25 minutes, depending upon whether saline or blood was given. Thereafter, there would be a gradual downward progression only momentarily reversed by fluid administration. This pattern would continue until the warming phase was begun, after which the pressure would rapidly return to the early bypass level. Following release of the occlusion clamps the pressure would again fall precipitously until a partial bypass was established after a regular heartbeat was reinstated by electroshock. In all experiments, the need for fluid was determined by depression of blood pressure below 60 mm. Hg. On discontinuing the bypass, the pressure was usually 40 to 50 mm. Hg below the normal preoperative level. The 6 normothermic dogs maintained a near posteannulation pressure during the entire bypass with a momentary depression following occlusion.

4. *Blood Studies.*—The results of blood studies are seen in Fig. 5. Gas studies were performed with a Van Slyke apparatus. Gas exchange and pH maintenance were satisfactory in all groups with the few exceptions mentioned below. Plasma hemoglobin levels did not reach excessive levels.

The widest fluctuation of pH was in Group C (45-minute occlusion) which was also the group with the highest survival rate. In this group, an average pH value of 7.64 was found following the 30-minute cooling period and 7.24 2 to 3 hours postoperatively. Postoperative acidosis was also evident in Group D and was severe (7.13) in the lowest survival group (E). No attempt was made to correct the pH other than by anticipatory variation of the respiratory rate.

Plasma hemoglobin values followed the expected linear relation to the length of the bypass. In only one group (E), with an average bypass length of 76 minutes, did the mean value exceed 100 mg. per cent. In contrast, Group C, in which bypass averaged 75 minutes, showed less than 100 mg. per cent. The variable in these two groups was an additional 15 minutes of cooling with myocardial ischemia in Group E.

Blood gas studies were unfortunately performed only in Groups A, C, and D. A diminution of both venous and arterial volume per cent CO_2 was seen in all groups except the postoperative samples in Group C, which showed marked elevations.

Satisfactory O_2 saturation was obtained in all cases except in the postoperative samples from Groups C and D. Group C showed a marked venous

anoxia of 42 per cent O_2 saturation with an acceptable arterial saturation of 88 per cent. Group D had a similar venous value with a markedly reduced arterial value of 66 per cent, indicating a danger in pulmonary cooling.

5. *General Observations.*—A dry ventricular field was obtained in all instances as shown by a bloodless right ventricle following cardiotomy. An aortotomy was performed in several early experiments which showed, after initial evacuation, a dry aortic valve and left ventricle.

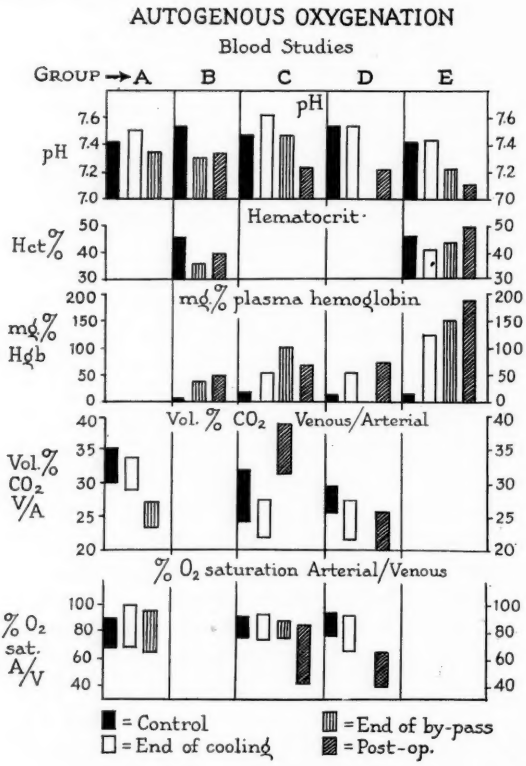

Fig. 5.

Pulmonary edema, as determined by endotracheal aspiration was seen in only 2 experiments; once following acute hemorrhage during cannula removal and once after a 3-minute period of severe shock due to pump failure before hypothermic induction. Both cases were in the pulmonary cooling group and the animals received large amounts of blood (500 c.c.) and saline (1,000 c.c.) to combat their shock.

The heart was seen to fibrillate and pass rapidly into hypothermic arrest at 22 to 25° C. during cooling. On rewarming, fibrillation occurred at 26 to 30° C. and would become quite strong above 30° C. following release of the

occlusion clamps. Defibrillation was accomplished with a 0.2 second 115 volt intermittent shock. The period of time required for defibrillation generally varied directly with the length of the occlusion period and seldom exceeded 2 minutes.

Three of the 4 dogs in Group B (normothermic), receiving potassium citrate for cardiac arrest, reverted to normal sinus rhythm following release of occluding clamps without requiring defibrillation. The 2 remaining dogs in this group, having received 200 mg. of acetylcholine, fibrillated during the first 10 minutes of the ventricular isolation period before arrest intervened. Defibrillating shocks were necessary to restore normal sinus rhythm after occlusion release. Electrocardiograms were taken postoperatively in several early experiments and revealed no alteration of the atrial conduction system.

DISCUSSION

The described bypass technique could be used for surgery of the ventricles, including outlet valves, coronary arteries, and ventricular septum below the endocardial cushion. Surgery of the remaining portions of the heart can be performed using a somewhat similar procedure developed in the same laboratory by Shields and Lewis[12] which involves profound hypothermia and circulatory arrest. Drew[6] has successfully applied this procedure clinically.

One of the outstanding features of this bypass technique is the small (600 c.c.) extracorporeal blood volume required. This minimizes the need for special blood preparations and, in some instances, the bypass priming blood could be drawn from the patient immediately before surgery.

Our closed system of bypass circuit eliminated much of the air embolism hazard ever present with heart-lung units and open circulation systems. Blood gas exchange was obviously not a problem.

The use of hypothermia avoided the dangers and difficulties incident to chemical cardiac arrest. The hazards of cardiac malfunction during hypothermia were avoided by partial bypass support during the cooling and rewarming stages.

Table II compares several of the more recent experimental studies on autogenous oxygenation.

TABLE II. EXPERIMENTAL AUTOGENOUS OXYGENATION STUDIES

AUTHOR	NUMBER OF DOGS	LENGTH BYPASS (MIN.)	LENGTH CARDIAC ISOLATION (MIN.)	TEMPERATURE	CARDIOTOMY	24-HOUR SURVIVAL
Cohen & Lillehei[4]	55	10-30	<30	normothermia	5 atria	50 (90%)
Blanco et al.[1]	13	30	none	normothermia	rt. ventricle	10 (77%)
Mustard et al.[9]	15	30-40	<30	normothermia	rt. ventricle	11 (73%)
Helmsworth et al.[7]	52	30	<30	normothermia	rt. ventricle	31 (59%)
Drew et al.[5, 6]	17	?	20-45* (6 dogs)	8-15° C.	?	4 (24%)
Shields & Lewis[12]	55	30-35	10-50*	<20° C.	11 ventricles	26 (47%)
Holt and Lewis	45	40-85	30-60	15° C.	rt. ventricle	31 (70%)

*Total circulatory arrest.

The four most troublesome technical aspects of this study follow:

1. *Arterial Occlusion Clamp.*—A clamp was sought which would totally occlude the ventricular inflow track without traumatizing the atria or seriously compromising their capacity, and which could be readily applied and removed without obstructing the surgical field. Numerous prototypes were tried, two of which are pictured in Fig. 4. Clamps similar to type *a* were applied with the least manipulation of the heart but caused more intra-atrial thrombosis, especially at the two points of compression reflection. Type *b* proved the least traumatic and effectively prevented blood flow to the ventricles. When tension was applied to the rubber tubing in this clamp, the atria were collapsed to some extent in a transverse as well as a longitudinal plane as seen in Fig. 4, *c*. A narrow rubber tube (1/8 in., outer diameter) was found necessary to prevent trauma to the vessels lying within the coronary sulcus and to minimize tension at the ventricular aspect of the auricular-atrial junction. Evidence of atrial trauma resulting from this clamp was a circumatrial ecchymosis and several instances of small (5 mm. diam.) organized intra-atrial thrombi. Although some atrial volume limitation was evident with both clamps, it was not considered serious. Neither clamp imposed restrictions on the immediate surgical field.

2. *Pulmonary Artery Cannulations.*—After trial with transventricular and direct arterial approaches, we found the direct arterial method more satisfactory. The technique which we employed is illustrated and described in Fig. 2.

3. *Arterial Cannulations.*—In the early experiments, considerable difficulty was encountered in preventing the atrial catheters from passing into the ventricles before applying the atrioventricular inflow clamp or preventing kinking of the catheters, especially in the left atrium, after clamping the atria. A solution to this problem and that of potential air embolism or blood loss around the catheters was found in the use of a multiperforated stainless steel tube, 5 cm. in length, inserted in the end of the catheter (Fig. 4, *d*). This rigid tip allowed manipulation of the catheter to provide a patent passage for drainage. The only indication of intra-atrial trauma from the metal insert tip was a localized ecchymosis at the site of prolonged contact in most short-term and several long-term survivors.

4. *Variation in Cardiac Cannulations.*—A partial solution to the problem of cardiac cannulation was found which has limited experimental application but significant clinical appeal. By utilizing a bilateral thoracotomy or median sternotomy approach, the right atrium is cannulated through the right external jugular vein, the left atrium from the right and anterior to the entrance of the right pulmonary veins, and the pulmonary and femoral arteries in the manner previously described. The higher mortality incident to bilateral thoracotomy which we have experienced in dogs precluded the use of this as a routine technique in our laboratory. With this cannulation approach, the pulmonary artery catheter is the only one in the field which can become an obstacle in ventricular surgery and the left atrial catheter is the only one requiring a cardiotomy for insertion. There is, however, an added danger of left atrial air

embolism due to leakage via the purse-string tie of the left atrial catheter. Mention might be made here that generally four catheters are used for pump-oxygenator bypass also.

CONCLUSION

We believe that our system satisfies the criteria for a successful autogenous oxygenation bypass as listed by Mustard,[9] such as (1) adequate oxygenation and exchange with total perfusion, (2) elimination of pulmonary venous obstruction, and (3) dry cardiotomy exposure.

Utilizing the described isolation and bypass system, all portions of the heart are rendered bloodless for surgery with the exception of the atria and the atrioventricular valves. This procedure can be readily modified to permit intra-atrial and atrioventricular valve surgery using the method described by Shields and Lewis[12] and Drew.[5, 6]

SUMMARY

1. Fifty dogs were subjected to bilateral total bypass with autogenous oxygenation and periods of ventricular isolation varying from 30 to 60 minutes while under profound hypothermia (44 dogs) or normothermia (6 dogs).

2. Variations in blood study values associated with a high mortality rate were found only in the group of dogs subjected to 60-minute ventricular ischemia.

3. The 24-hour survival rate in all experiments was 70 per cent and for over 1 week, 53 per cent. A 73 per cent long-term survival rate was obtained in the group with a 45-minute period of ventricular isolation (Group C).

4. Both ventricles, their outlet valves, and coronary arteries were rendered dry for open surgical repair.

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THE USE OF SILICONE IN MAINTAINING PATENCY IN DRAINAGE TUBES

George A. Harkins, M.D., San Francisco, Calif.*

IT HAS BEEN FOUND that blockage due to blood clot formation within chest drainage tubes has been avoided to a large extent by pretreatment of these tubes with silicone. Since adopting this measure 2 years ago, it has become unnecessary to milk the tubes frequently in order to maintain patency, and drainage failure in such catheters is a rarity. We have been unable to detect any harmful effect from the use of silicone for this purpose and believe it has added to the ease and safety of postoperative care.

The application of silicone is a simple matter and can be carried out with a large number of tubes simultaneously. In this hospital, the rubber tubes are washed, dipped into a bath of 5 per cent Silicone,† rinsed in distilled water, and baked in the oven until dry (10 to 20 minutes at 160° C.). Thereafter they are sterilized and used as necessary.

Pleural catheters siliconized in this manner have been used in more than 500 patients, and we can recommend the general adoption of this practice in thoracic surgery. In addition, pretreatment with silicone might afford better drainage in catheters placed following other operations, for example, after prostatectomy, radical neck dissection, and radical mastectomy.

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†Silicone, Z4141—Dow Corning Corp., Midland, Michigan.

CONSTITUTION OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

As Amended to May 12, 1960

Article I. Name

SECTION 1.—This Association shall be known as the American Association for Thoracic Surgery.

Article II. Object

SECTION 1.—The object of the Association shall be to encourage and stimulate investigation and study that will increase the knowledge of intrathoracic physiology, pathology, and therapy, to correlate such knowledge and disseminate it.

SECTION 2.—To attain this object, the Association shall hold at least one scientific meeting every year in which free discussion shall be featured; shall conduct a Journal for the publication of the papers presented at this meeting, and other acceptable articles; and shall undertake such other activities as the Council or the Association as a whole may decide.

Article III. Membership

SECTION 1.—There shall be four classes of members: Active, Associate, Senior, and Honorary. Admission to membership in the Association shall be by election. Membership shall be limited, the limits on the respective classes to be determined by the By-Laws. Only Active and Senior Members shall have the privilege of voting or holding elective office.

SECTION 2.—Election to Active, Senior, and Honorary Membership shall be for life, subject to the provisions of Section 3, following. After the 1960 Annual Meeting of the Association, election to Associate Membership shall be for a limited period of time, as determined by the By-Laws. During this limited period, an Associate Member, if properly qualified, may be elected to Active Membership. At the expiration of this limited period, an Associate Member, if not yet qualified for Active Membership, must either be reelected to an additional period of Associate Membership, or be dropped from the rolls of the Association.

SECTION 3.—Membership may be voluntarily terminated at any time by members in good standing. The Council, acting as a Board of Censors, may recommend the expulsion of a member on the grounds of moral or professional

delinquency, and submit his name, together with the grounds of complaint, to the Association as a whole at any of the regularly convened meetings, after giving the member so accused ample opportunity to appear in his own behalf.

Article IV. Officers and Government

SECTION 1.—The officers of the Association shall be a President, a Vice-President, a Secretary, a Treasurer, an Editor, and five Councilors. These ten officers and councilors shall be the governing body of the Association, and shall have full power to act on all matters, except as follows:

1. They may not alter the initiation fees or annual dues, nor levy any general assessments against the membership, except that they may, in individual cases, remit annual dues or assessments.

2. They may in no wise change the Constitution or By-Laws.

3. They may neither elect new members nor alter the status of existing members, other than to apply the provisions of Article III, Section 3.

4. They may not deplete the principal of the Endowment Fund.

SECTION 2.—Officers and Councilors shall be elected at the annual meeting of the Association, and shall take office upon conclusion of the meeting. The President and the Vice-President shall be elected for a one-year term of office and neither may be re-elected to succeed himself in the same office. The Secretary, the Treasurer, and the Editor shall be elected for a one-year term of office, and any or all may be re-elected indefinitely. The outgoing President shall automatically become a Councilor for a one-year term of office. The other four Councilors shall be elected, one each year, for a four-year term of office, but no Councilor may be re-elected to succeed himself.

SECTION 3.—Vacancies occurring among the officers and councilors during the year shall be temporarily filled by action of the Council, subject to approval of the Association at the next regularly convened meeting.

Article V. Committees

SECTION 1.—At the opening session of the annual meeting there shall be elected, after nomination from the floor of the Association, a Nominating Committee of three. This Committee shall prepare a slate of nominees for officers and councilors and shall present their report at the executive session of the Association.

SECTION 2.—The Council is empowered to appoint a Membership Committee, an Auditing Committee, a Program Committee, a Necrology Committee, and such other committees as may in its opinion be necessary. All such committees shall render their report at the executive session of the Association.

SECTION 3.—The Editor is empowered to appoint an Editorial Board, subject only to the approval of the Council.

SECTION 4.—The Association as a whole may authorize the Council to appoint Scientific or Research Committees for the purpose of investigating thoracic

problems and may further authorize the Council to support financially such committees to a limited degree. In appointing such committees, the Council shall be governed by the provisions of the By-Laws.

Article VI. Finances

SECTION 1.—The fiscal year of the Association shall run from the beginning of one annual meeting to the beginning of the next annual meeting. The books of the Association shall be kept and audited on this basis.

SECTION 2.—Members shall contribute to the financial maintenance of the Association through the medium of initiation fees, annual dues, and special assessments. The amount of the annual dues and the initiation fees shall be determined by the By-Laws.

If, at the end of any fiscal year, there be a deficit in the current funds of the Association, the Council may send out notices to that effect and invite Active members to contribute the necessary amount so that no deficit be carried over from one fiscal year to another. The Association may, in any regularly convened meeting, vote a special assessment for any purpose consistent with the objects of the Association (Article II), and such special assessment shall become an obligatory charge against the classes of members affected thereby.

SECTION 3.—To meet the current expenses of the Association, there shall be available all revenue derived from annual dues, special assessments, and income from Endowment Fund, subject to the provisions of Section 4, following. Funds derived from the payment of initiation fees shall not be available for current expenses.

SECTION 4.—All funds derived from the payment of initiation fees shall be placed in a special fund, to be invested and reinvested in legal securities, to be held intact, and to be known as the Endowment Fund. The Council is responsible for the proper management of the Endowment Fund, and may divert any surplus in the current funds of the Association into this fund, but may not withdraw any of the principal of the Endowment Fund except in accordance with the provisions of Section 6, following.

SECTION 5.—The income from the Endowment Fund shall be expended as the Council directs.

SECTION 6.—The principal of the Endowment Fund may be withdrawn, in whole or in part, under the following conditions only: The amount of principal to be withdrawn shall have been approved by the Council; it shall have been approved by a majority of the members present and voting at a regularly convened annual meeting; it shall have been tabled for one year; it shall have been finally passed by a three-fourths vote of the members present and voting at the next regularly convened annual meeting.

SECTION 7.—In the event of the dissolution of the Association, the Endowment Fund shall be distributed among national institutions of the United States and Canada in a proportion equal to the then existing ratio between the numbers of citizens of the two nations who are members of the Association.

Article VII. Meetings

SECTION 1.—The time, place, duration, and procedure of the annual meeting of the Association shall be determined by the Council, and the provisions of the By-Laws.

SECTION 2.—A special meeting of the Association may be called on one month's notice on the written request of fifteen members. The specific purposes of the meeting must be stated in the request and in the official call for the meeting.

SECTION 3.—The annual meeting of the Council shall be held at or near the close of the fiscal year.

Article VIII. Amendments

SECTION 1.—This Constitution shall in no wise be changed except by a three-fourths vote of the members present at an annual meeting, and further provided that the proposed alteration or amendment shall have been moved and seconded at a previous annual meeting, and that printed copies of the suggested alteration or amendment shall have been circulated among the members, and that the members shall have been specifically advised that such alteration or amendment will be voted upon.

BY-LAWS

Article I.

SECTION 1.—These By-Laws shall merely interpret the Constitution and specifically apply its principles. They shall set forth no principles not included in the Constitution.

Article II.

SECTION 1.—All papers read before the Association shall become the property of the Association. Authors shall leave original copies of their manuscripts with the Editor or Reporter, at the time of presentation, for publication in the official journal.

SECTION 2.—When the number of papers makes it desirable, the Council may require authors to present their papers in abstract, and may set a time limit on discussions.

SECTION 3.—Members are urged to cooperate with all Scientific Committees of the Association.

SECTION 4.—Attendance at Annual Meetings and participation in the scientific programs shall be optional for all Honorary and Senior Members, but it shall be expected from all Active and Associate Members.

SECTION 5.—While the scientific session of the annual meeting is held primarily for the benefit of the members of the Association, it may be thrown open to nonmembers who are able to submit satisfactory credentials, who register in a specified manner, and who pay such registration fee as may be determined and published by the Council from year to year.

ARTICLE III.

SECTION 1.—Candidates for membership in this Association must be formally nominated and seconded, in an approved manner, by not less than three Active or Senior Members. Such nomination must have been in the hands of the Membership Committee for not less than four months, and the name of the candidate must have been distributed to the Association as a whole before final action may be taken on any new candidate for election to Active or Associate Membership. Provided the foregoing requirements have been met, and the candidates have been approved by the Membership Committee and by the Council, their names shall be presented to the Association at a regularly convened annual meeting for final action. A three-fourths vote of those present and voting shall be required to elect. Any candidate for membership in this Association who has failed of election for two successive years shall automatically cease to be a candidate and may not be renominated until after a lapse of three years.

SECTION 2.—Active Membership shall be limited to three hundred fifty. The candidate, to be eligible, must be a citizen of the United States of America or of Canada, unless in unusual cases this citizenship requirement shall have been waived by the Council. The candidate shall have achieved distinction in the thoracic field, or shall have made a meritorious contribution to knowledge pertaining to thoracic disease or its surgical treatment. Under usual circumstances, Active Members shall be elected from the Associate Members who have satisfied all requirements for Active Membership. Under unusual circumstances, Active Membership may be awarded to new candidates of outstanding distinction.

SECTION 3.—There shall be no numerical limit on Associate Membership. The candidate, to be eligible, may be a citizen of any country. All candidates for Associate Membership shall be engaged actively in the practice of clinical medicine, or in teaching, or investigative work in the basic sciences underlying clinical practice, and all shall have demonstrated an active interest in thoracic disease. In the case of those who are engaged in the independent practice of thoracic surgery, it shall be required that they present evidence of sound basic training in general as well as thoracic surgery. Clinicians of outstanding ability, whose interest is limited to a small fraction of the entire thoracic field, may be elected to Associate Membership. The limited period of time for Associate Membership as required by Article III, Section 2, of the Constitution, shall be five years.

SECTION 4.—The number of Senior Members shall be unlimited. The candidate, to be eligible, must have been an Active Member of the Association for not less than ten years or, having been an Active Member, have passed the age of sixty years, or become incapacitated by illness.

SECTION 5.—Honorary Membership shall be reserved for such distinguished persons as may be deemed worthy of this honor by the Council with concurrence of the Association.

SECTION 6.—The report of the Membership Committee shall be rendered at the annual Executive Session of the Association. Candidates shall be presented

in groups in the following order: Candidates for Honorary Membership; retirement of Active Members to Senior Membership; candidates for Active Membership; candidates for Associate Membership.

SECTION 7.—The Council shall recommend that any Active or Associate Member whose dues are in arrears for two years, or who has been absent, without sufficient excuse, from three consecutive annual meetings, shall have his membership terminated.

SECTION 8.—Notwithstanding Section 7, any member of the Association over 60 years of age is excused from the attendance requirement and upon his specific request may likewise be excused from the payment of dues.

ARTICLE IV.

SECTION 1.—The President of the Association shall perform all duties customarily pertaining to the office of President. He shall not only preside at all meetings of the Association, but also at all meetings of the Council. The President shall be elected from the Active Members of the Association.

SECTION 2.—The Vice-President of the Association shall perform all duties customarily pertaining to the office of the Vice-President, not only as to the Association, but also as to the Council. The Vice-President shall be elected from the Active Members of the Association.

SECTION 3.—The Secretary of the Association shall perform all duties customarily pertaining to the office of Secretary. He shall serve not only as Secretary of the Association but also as Secretary of the Council. The Secretary shall be elected from the Active Members of the Association.

SECTION 4.—The Treasurer of the Association shall perform all duties pertaining to the office of Treasurer. He shall not only serve as Treasurer of the Association but shall also serve as custodian of the Endowment Fund. The Treasurer shall be elected from the Active Members of the Association.

SECTION 5.—The Editor of the Association shall be the Editor of the official Journal and shall, ex officio, be the Chairman of the Editorial Board. The Editor shall be elected from the Honorary, Active, or Senior Members of the Association.

SECTION 6.—The Councilors of the Association shall hold office as specified in the Constitution. They shall be elected from the Active or Senior Members of the Association.

SECTION 7.—In the event of a vacancy occurring in the office of President, the Council shall advance the Vice-President to the Presidency and appoint a new Vice-President under the Provisions of Article IV, Section 3, of the Constitution.

ARTICLE V.

SECTION 1.—The Nominating Committee shall consist of three Active or Senior Members who are, by preference, also past Presidents of the Association and in attendance at the meeting. They shall be elected in accordance with the provisions of Article V, Section 1, of the Constitution. The Council shall instruct the Committee as to the vacancies which are to be filled by election.

SECTION 2.—The Membership Committee shall consist of seven Active or Senior Members appointed in accordance with the provisions of Article V, Section 2, of the Constitution. The Council may appoint not more than one of its own members to serve on this Committee. The duties of the Membership Committee are to investigate all candidates for membership in the Association and to report their findings as expeditiously as possible to the Council through the Secretary of the Association. This Committee is also charged with searching the literature of this and other countries to the end that proper candidates may be presented to the Association for consideration. Appointment to this Committee shall be for a period of one year, and not more than five of the members may be reappointed to succeed themselves. This Committee is also charged with maintaining a record of membership attendance and participation in the scientific programs and reporting to the affected members and to the Council any deviations from the requirement of Article II, Section 4, of these By-Laws.

SECTION 3.—The Auditing Committee shall consist of three Active or Senior Members appointed in accordance with the provisions of Article V, Section 2, of the Constitution. None of these may be selected from the officers or councilors of the Association. Their duty shall be to audit the accounts of the Association at the end of each fiscal year and render their report to the Council of the Association through the Secretary. Appointments to this Committee shall be made for a one-year term. Not more than two members may be reappointed to succeed themselves.

SECTION 4.—The Program Committee shall consist of five members: The President of the Association, the Secretary of the Association, the Editor of the Association, and two members at large, one of whom shall be resident at or near the place of annual meeting. The duties of this Committee shall be to arrange, in conformity with instructions from the Council, the scientific program for the annual meeting.

SECTION 5.—The Necrology Committee shall consist of one or more Active or Senior Members, and shall be appointed in accordance with the provisions of Article V, Section 2, of the Constitution. Appointments to this Committee shall be for a one-year term of office. Any or all members of this Committee may be reappointed to succeed themselves. The Council may, if it so desires, appoint one of its own members to serve as Chairman of this Committee. The duties of the Necrology Committee shall be to prepare suitable resolutions and memorials upon the deaths of all members of the Association and to report such deaths at every annual meeting.

SECTION 6.—The Editorial Board shall be appointed by the Editor, subject only to the approval of the Council. The Editor shall be, ex officio, the chairman of this board and shall be privileged to appoint and indefinitely reappoint such members of the Association, regardless of class of membership, and such nonmembers of the Association as in his opinion may be best calculated to meet the editorial requirements of the Association.

SECTION 7.—When Scientific or Research Committees are authorized by the Association, the Council shall appoint the Chairmen of these Committees, with

power to organize their committees in any way best calculated to accomplish the desired object, subject only to the approval of the Council. Financial aid rendered to such Committees shall not exceed such annual or special appropriations as may be specifically voted for such purposes by the Association as a whole.

ARTICLE VI.

SECTION 1.—Honorary Members of the Association are exempt from all initiation fees, dues, and assessments.

SECTION 2.—Annual dues for Active Members shall be $30.00.

SECTION 3.—Annual dues for Associate Members shall be $25.00.

SECTION 4.—Senior Members are exempt from dues.

SECTION 5.—Initiation fee for those elected directly to Active Membership shall be $15.00.

SECTION 6.—Initiation fee for those elected to Associate Membership shall be $10.00. If and when an Associate Member is elected to Active Membership, he shall pay an additional $5.00 initiation fee.

SECTION 7.—Income from the Endowment Fund shall be expended as the Council directs.

SECTION 8.—Associate and Active Members must subscribe to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY to retain their membership status.

SECTION 9.—Senior Members may retain their membership status without the payment of annual dues and subscription to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY is optional.

(Note.—Bills for membership dues and for subscriptions to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY will be mailed to members by the Treasurer after the Annual Meeting.)

ARTICLE VII.

SECTION 1.—When the Association convenes for its annual meeting, it shall immediately go into executive session, but the business at this session shall be limited to:

1. Election of Nominating Committee.
2. Appointment of necessary committees.
3. Miscellaneous business of an urgent nature.

SECTION 2.—The annual executive session of the Association shall be held at the opening of the afternoon session of the second day of the meeting. The order of business shall be:

1. Reading of the minutes of the preceding meetings of the Association and Council.
2. Report of the Treasurer for the last fiscal year.
3. Report of the Auditing Committee.
4. Report of the Treasurer for the current year to date.
5. Report of the Necrology Committee.

6. Report of the Program Committee.
7. Action on amendments to the Constitution and By-Laws.
8. Action on recommendations emanating from the Council.
9. Unfinished Business.
10. New Business.
11. Report of the Membership Committee.
12. Election of new members.
13. Report of the Nominating Committee.
14. Election of officers.

SECTION 3.—At the annual meeting of the Council the order of business shall be:

1. Reading of minutes.
2. Treasurer's report.
3. Appointment of committees.
4. Determination of instructions to be given to Auditing, Membership, Necrology, and other committees except Program Committee.
5. Determination of details in connection with the annual meeting.
6. Appointment and instructions to the Program Committee.
7. Unfinished Business.
8. New Business.

SECTION 4.—There shall be an annual meeting of the Council.

ARTICLE VIII.

SECTION 1.—These By-Laws shall in no wise be changed except by a two-thirds vote of the members present at the annual meeting or a properly convened meeting of the Association, and further provided that the proposed action or amendment shall have been moved and seconded by not less than three of the members in a properly convened annual or special meeting of the Association.

SECTION 2.—These By-Laws may be suspended in whole or in part for a period of not more than twelve hours by a unanimous vote of those present at any regularly convened meeting of the Association.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-first Annual Meeting of The American Association for Thoracic Surgery will be held April 24, 25, and 26, 1961, in Philadelphia, Pennsylvania. Headquarters will be the Sheraton Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mr. Brian Kirby, Reservation Manager, Sheraton Hotel, Philadelphia 3, Pennsylvania. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1961 meeting *must be received on or before* **November 15, 1960,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis (Clayton) 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1960,** otherwise the application will be deferred for consideration until the 1962 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Presbyterian Medical Center
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*